OMB No. 0990-0115

# Electronic Request for Proposal

## SECTION A – SOLICITATION/CONTRACT FORM

**OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE http://www.niaid.nih.gov/contract/default.htm FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.**

| **Purchase Authority: Public Law 92-218, as amended.**<br>**NOTE: The issuance of this solicitation does not commit the government to an award.** | | | |
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| ***RFP Number:***<br>NIH-NIAID-DMID-03-09 | ***Just In Time:***<br>[ ] Yes<br>[ X ] No | Small Bus. Set-Aside [ ]Yes [X]No<br>8(a) Set-Aside [ ]Yes [ X ]No<br>NAICS Code: 54171<br>Size Standard: 500 employees | ***Level of Effort:***<br>[ ] Yes [X] No<br>***Total Effort:***<br>[ ] |
| ***TITLE:*** New Animal Models for: Part A Tuberculosis (TB); and Part B Invasive Aspergillosis (IA) | | | |
| ***Issue Date: May 2, 2002*** | ***Due Date:*** ***August 12, 2002***<br>***Time:*** **4:00 PM, EST** | | ***Technical Proposal Page Limits:***<br>[ X ] Yes *(see "How to Prepare and Submit Electronic Proposals")*<br>[ ] No |

| ***ISSUED BY:*** | [X] ***We reserve the right to make awards without discussion.*** | |
|---|---|---|
| Paul D. McFarlane<br>Contracting Officer<br>Contract Management Branch, DEA<br>NIH, NIAID<br>6700-B Rockledge Drive<br>Room 2230, MSC 7612<br>Bethesda, MD 20892-7612 | ***NO. OF AWARDS:***<br>[ ] Only 1 Award<br>[X] Multiple Awards | ***PERIOD OF PERFORMANCE:***<br>7 years beginning on or about 03/03/2003 |

Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See SECTION J - Attachments)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. The paper copy with original signatures is the official copy for recording timely receipt. If the paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

***POINT OF CONTACT*** **-- Ross Kelley** ***--COLLECT CALLS WILL NOT BE ACCEPTED--***

| ***Telephone:*** ***Direct*** **301-402-2234**<br>***Main*** **301-496-0612** | ***Fax*** **301-402-0972** | ***E-Mail*** **rkelley@niaid.nih.gov** |
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**BACKGROUND / STATEMENT OF WORK / NOTES TO OFFERORS**

New Animal Models for TB and Invasive Aspergillosis (IA) Post Genomic Research
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This contract is in support of the NIAID's research agenda to further the understanding of the pathogenesis of bacterial and fungal infections. This agenda encompasses all aspects of basic and translational research from genomics initiatives to clinical studies. Recently, the NIAID established a functional genomics resource center at The Institute for Genomic Research (TIGR) in Rockville, MD. ( http://pfgrc.tigr.org ). The center will provide tools, reagents and training for researchers and will play a key role in helping scientists use an organism's DNA code to learn new ways to address that organism. It is anticipated that a large amount of genomic information will become available as a result of the availability of these resources, the successful completion of the sequencing many bacterial genomes, including *Mycobacterium tuberculosis* (Mtb) and ongoing efforts to sequence more complex microbial pathogens such as *Aspergillus fumigatus.* This information will be used to provide primary annotation and putative assignments of genes and will lead to the identification of genes that may have potential as drug targets or may present candidates for diagnostics development or immunological interventions, such as vaccines. However, since these selections are based on theoretical and comparative analyses *in silico*, the utility of many of these genes remains to be validated. Steps in this validation process include expression and characterization of the gene product. As an example, the NIAID supported TB Structural Genomics Consortium ( http://www.doe-mbi.ucla.edu/TB) aims at determining the 3-dimensional structure of over 400 mycobacterial genes and these studies are likely to produce a large number of potential gene targets that will warrant further analysis. Eventually, after structural and biochemical characterization, target genes will have to be validated in animal models of bacterial or fungal infection to determine what role these microbial genes play in the survival of the pathogens in the host or the progression of infection and disease. Although a number of animal models and resources (www.mmrrc.org/index.html ) are already available, these models are best suited to study various stages of bacterial and fungal infection and disease, as well as immunological parameters. However, since these models are often very complex and time consuming, they may be of limited suitability to validate a large number of gene candidates in short succession in a more rapid manner, as will be necessary to keep up with the pace of post-genomic research.

This contract is intended to provide a development and resource platform for animal models of tuberculosis and invasive aspergillosis that will be made available to qualified researchers and will allow high throughput evaluation of target genes *in vivo*. As such, this contract solicits separate proposals for the development of animal models of tuberculosis (Part A) and development of animal models of invasive aspergillosis (Part B). Offerors can apply for either Part A or Part B, or both. Offerors submitting proposals for both Part A and Part B are required to submit a separate business and technical proposal for Part A and a separate business and technical proposal for Part B.

Tuberculosis, even in the new millennium, represents a major global health burden. One third of the world population is infected with Mtb and 1 in 10 of these individuals will likely develop active disease. Available multi-drug therapy can essentially treat tuberculosis, but the standard regimens are complicated and lengthy, leading to difficult implementation and poor compliance. In light of this difficulty and the increased spread of multi-drug resistant tuberculosis it is obvious that there is a need for novel treatment approaches and new chemotherapeutic agents to better control this disease. Furthermore, since the ultimate solution for eradication of tuberculosis lies in the development of an efficacious vaccine, rational vaccine design, in addition to identification of drug targets from genomic information, may open the door to new approaches to combat this disease.

The important role of animal models in TB drug research and development, as part of a comprehensive NIAID program in Tuberculosis, was highlighted in the recently published Scientific Blueprint for TB Drug Development (Tuberculosis 2001, 81:supp1) and was recognized by the NIAID Infectious Disease Drug Development Summit (September 26-27, 2000, www.niaid.nih.gov/dmid/drug/execsum.htm ). Currently, models of Mtb infection and tuberculosis are available in a variety of small animal species and are also being developed in non-human primates. Some of these are available to the research community for testing of vaccine and drug candidates (www.cvmbs.colostate.edu/microbiology/tb/top.htm , http://www.taacf.org/).

While these models are well characterized and designed to answer critical questions in infection, disease and host immunity, they need to be adapted to allow more rapid evaluation of the function of mycobacterial genes in the host. **Part A** of this contract seeks to solicit proposals for creating and performing rapid throughput models as a service to the research community. These models are to produce preliminary information about whether target genes are essential for the survival of Mtb in the host, about how these genes affect the interactions of host and microbe, and whether expression of mycobacterial target genes affects host responses. This will require not just the establishment of optimized animal systems, but also the generation and application of molecular genetic tools to allow rapid cloning of target genes into virulent Mtb species to assess gene function *in vivo*. Since gene knock out strategies in Mtb will not be a viable option for assessing functions of essential genes, molecular strategies to either alter the activity of these genes, or regulate their expression *in vivo* will have to be part of the overall design of rapid throughput models. It will be a challenge to develop models that are suitable to keep pace with the speed that information is generated from genomic and postgenomic efforts. This challenge may require that not just one animal model system, but rather multiple systems be utilized separately to produce a cohesive set of data that will allow preliminary assessment of the role of mycobacterial genes in infection and disease. **Part A** of this contract should produce information for the research community as a whole that will serve to stimulate more in depth research into the functional details of critical genes in Mtb and eventually lead to the selection of novel drug targets, vaccine candidates or ideas for diagnostic tools, thereby filling a critical gap in the path from genomic to translational research in tuberculosis.

Invasive aspergillosis (IA) is the most critical unmet medical mycological challenge as assessed by the five part NIAID Mycology Workshop Series ( www.niaid.nih.gov/dmid/meetings ), and the Summit on Development of Infectious Disease Therapeutics ( www.niaid.nih.gov/dmid/drug/execsum.htm ). Although it is a subject of intensive study by the European Organization for Research and Treatment of Cancer and the NIAID Bacteriology and Mycology Study Group (BAMSG), it remains a leading cause of infectious mortality in organ and bone marrow transplant patients. In the most vulnerable clinical groups, mortality from IA can approach 100% and one study estimated 10,000 cases of IA per year in the US. Furthermore, two studies documented IA-consistent histopathology in 4% of all deaths in autopsy surveys. In one of the two studies, IA was not considered as a diagnosis prior to death in over 50% of the cases.

One of the most challenging aspects of studying this disease is the lack of effective diagnostic methods, and the inability to isolate the fungus from blood in a reliable manner. Clearly, the development of a diagnostic for early detection of IA would facilitate not only better treatment, but also the design of future studies for treatment of IA.

Research in IA is also difficult to conduct from a more practical standpoint. *Aspergillus fumigatus*, the most frequent etiologic agent, is a filamentous fungal saprophyte that sporulates readily and is ubiquitous, even in hospitals. The ability to culture *A. fumigatus* from non-sterile sites in patients does not constitute a diagnosis since *A. fumigatus* can also be cultured from these sites in healthy individuals. The development of surrogate immunological markers of infection could be complicated by previous exposure and by altered immune status at the time of testing. Additionally, the invasive filamentous growth form of the fungus complicates efforts to quantify fungal growth and disease progression *in vivo*.

**Part B** of this contract is to help advance the understanding of this life-threatening disease by refining and standardizing animal models of infection to allow reliable quantification of infectious burden or to define surrogate markers of infection and disease progression. Success in establishing and implementing the use of clinically relevant and experimentally tractable models will depend upon the assembly of an integrated team offering expertise in animal modeling, mycology, and molecular and genomic technologies. To benefit from genomic information that will become available in the public domain, these animal models should be developed using *A. fumigatus*. However, given the wealth of available genetics in the mycologically similar filamentous model organisms, *Aspergillus nidulans* and *Neurospora crassa* (the latter is currently being sequenced for the public domain), great potential exists for expanding expertise in the research community to the critical mass necessary to make rapid advances in IA. Therefore, close interaction with expert panels to identify gaps and research opportunities in IA will be key to the successful adaptation of currently available animal models of aspergillosis. Once these models have been refined and standardized, they will be made available to the research community to answer key scientific questions and validate information that is expected from the sequencing of *Aspergillus fumigatus* and related genomes.

**Statement of Work**
**New Animal Models for: Part A Tuberculosis (TB) and Part B Invasive Aspergillosis (IA)**
**RFP DMID-03-09**
**(GENERAL NOTE TO OFFEROR)**

# Part A – New Animal Models for Tuberculosis

Independently and not as an agent of the Government, the Contractor shall furnish all necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government as needed to perform this Statement of Work.

Specifically, the Contractor, with the approval of the Project Officer, shall:

1) Develop improved animal models of tuberculosis that closely mimic different stages of human *M. tuberculosis* (Mtb) infection, as well as TB disease. These models are to be improved to facilitate evaluation, in a rapid throughput format, of Mtb genes identified from genomic and post-genomic efforts. To guide development of these animal models and to judge progress, the contractor shall, no later than three months after contract award, provide a list of detailed milestones, timelines and decision criteria to assess satisfactory completion of each milestone. These milestones will be developed together with the Project Officer and an expert panel of advisors. The expert panel of advisors will be established by the Project Officer with input from the contractor no later than three months after contract award. Some members of this panel will specifically advise the Project Officer, and all members will advise the contractor on all aspects of science and progress throughout the term of the contract.

   *New models shall:*
   a) utilize virulent *Mycobacterium tuberculosis* strains and may involve other mycobacterial species if sufficient rationale for their suitability is provided;
   b) be based on currently accepted models of tuberculosis in small rodents or rabbits;
   c) answer specific questions about different stages of Mtb pathogenicity, such as establishment of infection, latency, granuloma formation and reactivation which may require development of more than one model;
   d) be suitable for rapid-throughput evaluation of gene function (i.e. in a more efficient manner than possible with current models); it is assumed that at least 100 genes will be evaluated;
   e) include histological and immunological characterizations to answer whether Mtb genes play a role in host-pathogen interactions and specific host response;
   f) be developed and validated utilizing genes with known and distinct function in mycobacterial survival, host-pathogen interaction and host response to infection;
   g) include development of molecular genetic strategies to facilitate rapid engineering of Mtb or other proposed mycobacterial strains, to allow cloning and expression of target genes for later evaluation in the animal host; strategies shall be considered that employ alternatives to gene knockout in mycobacteria, such as expression under the control of *in vivo* regulatable promoters or introduction of mutations to alter the activity of a gene product;
   h) possibly be amenable to gene profiling studies at various stages of infection and during various stages of disease;
   i) be developed within a timeframe of approximately 2 years. **(NOTE 1 TO OFFEROR)**

2) Upon completion of the development phase, and no later than 3 months after the completion of the last development milestone, and in addition to regular reporting requirements, the contractor shall provide to the Project Officer a comprehensive report outlining the composition of all

developed models, detailed standardized procedures for their implementation (SOPs), including genetic engineering protocols and all quality control measures. This shall also include a plan for how the contractor will perform these models as a service to the community. Acceptance of these SOPs will be by the Project Officer after consultation with the expert panel.

This report will address:

a) procedures for receiving and prioritizing genes submitted by qualified investigators, including the contractor;
b) procedures for qualified outside investigators to apply for testing of genes in these newly developed models;
c) procedures for interaction with the community (such as web-sites, presentations at scientific meetings, etc.) to solicit gene submissions for testing;
d) what types of information will be required from the outside investigator to allow rapid evaluation of the submitted genes in the animal model(s);
e) quality control criteria for each assay/model/molecular approach;
f) criteria for choosing bacterial and animal strains for testing;
g) decision criteria for selection of various models on the basis of what is known about a submitted gene (i.e. similarity to genes with known function, putative placement in biochemical pathways and role of these pathways in bacterial virulence and host-pathogen interaction etc.);
h) how all genetic tools, constructs and possibly animals that have been developed under this contract will be provided to qualified investigators in the research community and the NIAID;
i) what types of reports will be provided to investigators;
j) how confidentiality of research results and protection of research interests of the submittor will be assured;
k) safety and proper handling procedures for using pathogens, animals and reagents employed in the models.**(NOTE 2 TO OFFEROR)**

3) Test the function of gene products identified through research efforts including, but not limited to genomic and proteomic approaches, as a service to the community. Prioritization of genes for testing, and selection of the appropriate animal models will be approved by the Project Officer with input from the expert panel of advisors.
   a) Provide a research and administrative team that includes all expertise needed for implementation of contract testing of gene functions *in vivo*, including animal model and molecular biology expertise.
   b) Provide resources and qualified personnel to clone genes in molecular systems developed for this contract that are suitable for analyzing Mtb genes in the host animal.
   c) Consider all available information for a given gene to select the appropriate animal model. Provide resources and qualified personnel to evaluate the cloned genes in the appropriate animal models of infections, developed under this contract, to assess whether genes play a role in infection, host-pathogen interactions and specific host response; this shall be done in close collaboration and discussion with the external researchers that submitted the genes;
   d) Routine testing of gene function is to comprise at least 50% of the total contract effort.
   e) Provide to the community all genetic constructs, bacterial and animal strains developed and constructed under this contract; additionally, provide these materials to NIAID for storage and further distribution;
   f) Assure close collaboration and interaction with research laboratories producing genomic and post-genomic information for Mtb;
   g) Adequately network within the research community to raise awareness for this contract resource and attend one national or international meeting per year for this purpose;

h) Report progress and all testing activities and results according to “Deliverables and Reporting Requirements” in this contract.
i) For each gene evaluation, provide a detailed report to the investigators who are submitting the genes. **(NOTE 3 TO OFFEROR)**

4) Upon request, and after consultation with the Project Officer and the panel of experts, provide protocols for further optimization and expansion of the models. These optimizations shall be performed in parallel to the models being conducted as a service to the community. The proposed protocols are subject to approval by the Project Officer.**(NOTE 4 TO OFFEROR)**

5) Provide reports and meet with the Project Officer at agreed upon intervals (refer to the "Deliverables and Reporting Requirements" in this contract).**(NOTE 5 TO OFFEROR)**

6) Organize and conduct one one-day workshop per year to discuss scientific topics related to functional analysis of genes in animal models, as approved by the Project Officer.**(NOTE 6 TO OFFEROR)**

7) Provide safe facilities and resources in accordance with Attachment A.1. of the STATEMENT OF WORK for Part A. The Attachment is entitled “SAFETY CONTROLS AND STANDARDS."

a) Conduct work under this contract under BSL3 guidelines when working with virulent Mtb strains or when otherwise appropriate. Conduct all work in accordance with applicable Federal, state and local laws, codes, ordinances and regulations.
b) Provide safe facilities and equipment to receive, send to outside investigators and the NIAID, store, and manipulate infectious Mtb.
c) Provide protective garments, equipment and sufficient monitoring to assure safe handling of potentially hazardous microorganisms and materials. Specifically, the contractor shall comply with all applicable health and safety regulations while conducting the work set forth herein.

8) Provide training in the use of the developed animal model(s) and molecular techniques to qualified investigators, as negotiated with and approved by the Project Officer.**(NOTE 7 TO OFFEROR)**

**ATTACHMENT A.1.**

**STATEMENT OF WORK - Part A**

## SAFETY CONTROLS AND STANDARDS

In order to provide safety controls for protection of the life and health of employees and other persons; for prevention of damage to all property, and for avoidance of work interruptions in the performance of the contract, the Contractor and any subcontractors shall comply with the following standards or subsequent issues or any supplements. In addition, the Contractor shall comply with all applicable Federal, state and local laws, codes, ordinances and regulations, including obtaining of all required licenses and permits in connection with biological and hazardous materials.

(1) The Biosafety Microbiological and Biomedical Laboratory Guidelines, Centers for Disease Control and Prevention and the National Institutes of Health, third edition, HHS Pub. No. (CDC) 93-8395 published by the U.S. Government Printing Office, May 1993, stock number 17-040-00523-7.

(2) Recommendations for the Safe Handling of Cytotoxic Drugs, NIH Publication No. 92-2621.

(3) NIH Guidelines for the Laboratory Use of Chemical Carcinogens, NIH Publication No. 81-2385.

Copies of the above may be obtained from the Government Printing Office or:

Division of Safety
Office of Research Services
National Institutes of Health Building 31-Room 1C02
Bethesda , Maryland 20892
301-496-2960

(4) SAFETY AND HEALTH CLAUSE

(a) In order to help ensure the protection of the life and health of all persons, as well as to help prevent damage to property, the Contractor shall comply with all Federal, State, and local laws and regulations applicable to the work being performed under the contract. These laws are implemented and/or enforced by the Environmental Protection Agency, Occupational Safety and Health Administration, and other agencies at the Federal, State, and local levels (Federal, State, and local regulatory/enforcement agencies).

(b) Further, the Contractor shall take or cause to be taken such additional safety measures as the Contracting Officer, in conjunction with the project or other appropriate officers, determines to be reasonably necessary. If compliance with such additional safety measures results in an increase or decrease in the cost or time required of performance of any part of work under this contract, an equitable adjustment will be made in accordance with whichever applicable "Changes" Clause as set forth in this contract (FAR 52.243-1, Changes-Fixed Price; FAR 52.243-2, Changes-Cost-Reimbursement; or FAR 52.243-3, Changes-Time and Materials or Labor-Hours).

(c) The Contractor shall maintain an accurate record of, and promptly report to the Contracting Officer, all accidents or incidents resulting in the exposure of persons to toxic substances, hazardous materials or hazardous operations; the injury or death of any person; and/or damage to property incidental to work performed under the contact and all violations for which the Contractor has been cited by any Federal, State, or local regulatory/enforcement agency. The report shall include a copy of the notice of violation and the findings of any inquiry or inspection, and an analysis addressing the impact these violations may have on the work remaining to be performed. The report shall also state the required action(s), if any, to be taken to correct any violation(s) noted by the Federal, State, or local regulatory/enforcement agency and the time frame allowed by the agency to accomplish the necessary corrective action.

(d) If the Contractor fails or refuses to comply promptly with the Federal, State, or local regulatory/enforcement agency's directive(s) regarding any violation(s) and prescribed corrective action(s), the Contracting Officer may issue an order stopping all or part of the work until satisfactory corrective action (as approved by the Federal, State, or local regulatory/enforcement agencies) has been taken and documented to the Contracting Officer. No part of the time lost due to any such stop work order shall be subject to a claim for extension of time or costs or damages by the Contractor.

(e) The Contractor shall insert the substance of this clause in each subcontract involving toxic substances, hazardous materials, or hazardous operations. Compliance with the provisions of this clause by subcontractors will be the responsibility of the Contractor.

## Part B – New Animal Models for Invasive Aspergillosis (IA)

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government as needed to perform this Statement of Work.

Specifically, the Contractor, with the approval of the Project Officer, shall:

1) Within three months of contract award, establish, as approved by the Project Officer, a steering committee composed of experts from the field of aspergillosis, mycology, animal model development and fungal genetics to advise on critical aspects of animal model development for invasive aspergillosis. A meeting with this committee shall be conducted at least once per year.**(NOTE 1 TO OFFEROR)**

2) Within 6 months of contract award, organize and conduct a one day workshop, under the direction of the Project Officer, to identify critical gaps in aspergillosis research relating to animal model development/requirements.**(NOTE 2 TO OFFEROR)**

3) Optimize and refine, through consultation with the steering committee, existing small animal models of invasive aspergillosis to provide standardized model(s) suitable to address key scientific questions. To guide development of these animal models and to judge progress, the contractor shall, no later than three months after contract award, provide a list of detailed milestones, timelines and decision criteria to assess satisfactory completion of each milestone. These milestones will be developed together with the Project Officer and an expert panel of advisors. The expert panel of advisors will be established by the Project Officer with input from the contractor no later than three months after contract award.

New models shall:

a) be based on currently accepted models of IA in mice and may include one larger species such as rabbits, and shall include pulmonary challenge;
b) include neutropenic and immune-competent animals;
c) in at least one, allow continuous blood sampling for the detection of surrogate markers of infection or disease;
d) target survival times suitable to characterize surrogate markers of infection and disease progression (4-7 days);
e) be able to differentiate among prior exposure, colonization and infection;
f) allow reliable quantification of fungal burden by direct or indirect means and definition of surrogate markers of infection and disease progression, such as fever curves, detection of fungal metabolites etc. to overcome the limitations of quantitative organ cultures with filamentous fungi;
g) allow assessment and quantification of growth dynamics of filamentous fungi;
h) have the potential to be standardized;
i) answer questions specific to different disease stages of IA, such as infection and dissemination, which may require development of separate models;
j) shall be developed with *Aspergillus fumigatus* but also be suitable to evaluate virulence of various other *Aspergillus* species*;*
k) consider the use of telemetry or infrared monitoring to establish fever curves;
l) consider genomic information to develop molecular diagnostics approaches;
m) yield information about the role of *Aspergillus fumigatus* genes for survival and dissemination of the fungus in the host, host-pathogen interaction and host response to infection;

n) be amenable to gene profiling studies at various stages of infection and during various stages of disease;
o) use molecular genetics and cloning strategies to target and evaluate specific genes in the animal models;
p) be developed within a timeframe of approximately 2 years.**(NOTE 3 TO OFFEROR)**

4) Upon completion of the development phase, and no later than 3 months after the completion of the last development milestone, and in addition to regular reporting requirements, the contractor shall provide to the Project Officer a comprehensive report outlining the composition of all developed models, detailed standardized procedures for their implementation (SOPs), including genetic engineering protocols and all quality control measures. This shall also include a plan for how the contractor will perform these models as a service to the community. Acceptance of these SOPs will be by the Project Officer after consultation with the expert panel.

This report will address:

a) how best to identify key unanswered scientific questions and establish research priorities based on public health need, scientific opportunities and advances in aspergillosis research;
b) interactions with the steering committee and the scientific community to identify further research gaps and provide a prioritized research agenda;
c) procedures for receiving and prioritizing research questions to be addressed with the models developed under this contract; these research questions will be submitted by qualified investigators, including the contractor;
d) procedures for interaction with the community (such as web-sites, presentations at scientific meetings, etc.) to solicit input for the research agenda and provide hypotheses for evaluation in the newly adapted animal models;
e) quality control criteria and choice of fungal and animals strains;
f) decision criteria for selection of various models to answer specific research questions (role of specific genes in fungal virulence and host-pathogen interaction, decision criteria that will be applied to select the best model(s) to evaluate the questions/hypotheses);
g) how all genetic tools, constructs and possibly animals that have been developed under this contract will be provided to qualified investigators in the research community and the NIAID;
h) what types of reports will be provided to summarize research findings;
i) how confidentiality of research results and protection of research interests of the submittor will be assured;
j) safety and proper handling procedures for using pathogens, animals and reagents employed in the models.**(NOTE 4 TO OFFEROR)**

5) Utilize the standardized models to answer key scientific questions in IA with an emphasis on the identification of surrogate markers of infection and disease progression as posed by qualified investigators and the contractor, and approved by the Project Officer and the NIAID IA expert panel.

a) Provide a research and administrative team that includes all expertise needed to implement contract testing, including animal model and molecular biology expertise;
b) Provide resources and qualified personnel to perform standardized models for the IA research community; this shall include expertise in animal models, molecular biology and fungal genetics. This activity is to be at least 50% of the total contract effort for Part B;
c) Conduct specific experiments using the developed model(s) and related techniques as a service to qualified investigators.

d) Provide to the community all genetic constructs, bacterial and animal strains developed and constructed under this contract; additionally, provide these materials to NIAID for storage and further distribution;

**e)** Adequately network within the research community to raise awareness for this contract resource. **(NOTE 5 TO OFFEROR)**

6) Upon request, and after consultation with the Project Officer and the expert panel of advisors, provide protocols for further optimization and expansion of the models. These optimizations shall be performed in parallel to the models being conducted as a service to the community. The proposed protocols are subject to approval by the Project Officer. **(NOTE 6 TO OFFEROR)**

7) Provide reports and meet with the Project Officer at agreed upon intervals (refer to the "Deliverables and Reporting Requirements" in this contract).**(NOTE 7 TO OFFEROR)**

8) Conduct one one-day workshop per year to discuss scientific topics concerning IA and related animal models, as approved by the Project Officer.**(NOTE 8 TO OFFEROR)**

9) Provide training in the establishment of the developed animal model(s) and molecular techniques to qualified investigators, as negotiated with and approved by the Project Officer. **(NOTE 9 TO OFFEROR)**

**Notes To Offerors**

New Animal Models for TB and Invasive Aspergillosis (IA) Post Genomic Research
**DMID-03-09**

**GENERAL NOTE TO OFFEROR:** In responding to this RFP, offerors must describe in detail any technical approach and proposed methods to develop animal models as listed in the work statement, The offeror must also list the responsibilities and level of effort of all proposed personnel who will be assigned to the contract. Documentation shall be provided on the qualifications, experience, education, competence, availability (in relation to other commitments), and decision making authority of the principal investigator, key personnel, sub-contractors, as well as technical and support staff. Offerors must also provide necessary facilities, including all major equipment, animals (animal welfare assurances), and capabilities to perform all the functions of this work statement. See MANDATORY QUALIFICATION CRITERIA regarding animal facilities. Offerors are encouraged to propose sub-contracts with qualified researchers to provide cross disciplinary expertise. If a sub-contractor is proposed, the same technical information shall be provided as part of the proposal as is required of the prime contractor, i.e. the qualifications, experience, education, competence and availability (in relation to other commitments) of the Principal Investigator, key personnel and technical and support staff. The handling and transportation of all reagents and government-owned property under this contract shall be in accordance with all applicable local, state and Federal regulations including health and safety standards. (See attachment for the safety and health clause).

**PART A: NEW ANIMAL MODELS FOR TUBERCULOSIS**

**NOTE 1 TO OFFEROR:** The offeror must, at the time of the proposal, have demonstrable expertise in working with animal models of tuberculosis and genetic manipulation of mycobacteria. For this, the proposal shall contain specific descriptions of all scientific methods and techniques used to develop genetic systems and animal models that allow the analysis of mycobacterial genes in infection and disease. The offeror shall specifically address how the proposed methods and techniques will be used to determine the function of Mtb genes in an animal host in a rapid throughput manner. This shall include a detailed research plan and a description of all immunological and histological methods, all methods related to infection of animals and characterization/quantitation of Mtb growth *in vivo*, and shall also include a description of the genetic systems used to clone target genes, and how these systems are appropriate to facilitate evaluation of gene products *in vivo*. The proposal shall include 2 alternative strategies for the development of the model(s). The primary proposed model(s) and the alternative strategies are to be described on the basis of expected outcomes and should use as examples genes with known function in Mtb infection and disease. Any preliminary data already available to substantiate these proposals shall be included. Proposals shall specifically address how currently available models will be modified to allow evaluation of a large number of putative target genes in a rapid throughput manner. For work with virulent Mtb, the offeror must, at the time of the proposal, either have access to appropriate animal facilities for studies under BSL3 conditions (see MANDATORY QUALIFICATION CRITERIA), and shall provide documentation to this respect, or shall provide documentation clearly stating any arrangements that have been made to assure these facilities will be available at the start of the contract. Without this information, proposals will not be considered any further for award. The development of the models should be completed in approximately 2 years. If gene profiling studies are part of the proposal, equipment, including computing infrastructure must be available at the time of the proposal and must be listed in the proposal. After award, the Program Officer, with input from the contractor will establish an expert panel of advisors. The offeror is **not** to suggest names of individuals for inclusion in the expert panel in the proposal. For the purpose of preparing a cost proposal, assume that the expert panel will be comprised of 5-6 individuals, 1-2 of whom may be international scientists. Assume that travel costs and per diem will be provided for this panel and that consultations with this panel will be part of the annual meeting with the Project Officer in Bethesda, MD (see NOTE 5 and NOTE 6 TO OFFEROR). Back to Item 1 of the Statement of Work.

**NOTE 2 TO OFFEROR:** The contractor shall provide detailed standard operating procedures (SOPs) for the utilization of the newly developed model(s) for routine evaluation of the function of target genes. These SOPs shall include quality control criteria, choice of bacterial and animal strains, decision criteria that will be applied to select the best model(s) for evaluation of particular genes. It shall include procedures for qualified outside investigators and the contractor to apply for testing of genes in these newly developed animal models. It shall also include design of internet websites, discussions with outside investigators regarding the appropriate choice of models, and what types of reports the contractor will provide to summarize the test findings. Procedures to assure confidentiality of research results must be included. These SOPs are considered deliverables under the contract (see Deliverables and Reporting Requirements). As part of the proposal, the offeror shall submit a draft outlining the above SOPs and shall utilize the proposed model systems as the basis and example for developing these criteria. This draft will be used in the evaluation of the contract proposal but the procedures outlined in the draft may not be the experiments/procedures that will be approved in the contract. Back to Item 2 of Statement of Work

**NOTE 3 TO OFFEROR:** It is expected that at least 100 target genes will need to be evaluated during the term of the contract. To consider all available information for a given gene, close collaboration with investigators submitting genes, as

well as networking within the research community is required. To assure adequate networking capabilities, for the purpose of preparing a cost proposal, assume attendance of one international or national meeting per year by one key personnel. Also assume that 2 key personnel will attend a total of one other scientific meeting per year or that 1 key personnel will attend a total of 2 other scientific meetings per year to maintain interactions with the scientific community. Back to Item 3 of Statement of work.

**NOTE 4 TO OFFEROR:** It is conceivable that new technologies and data will become available during the lifetime of this contract. Therefore, the contractor may propose optimizations or extensions of the models. These optimizations and further research on these models must be negotiated and will be subject to approval by the Project Officer. The extent and timing of these proposals will be determined by the Project Officer and will be communicated to the contractor at the appropriate time.

**NOTE 5 TO OFFEROR:** For the purpose of preparing a cost proposal, assume that one or two key personnel will make one visit per year to Bethesda, MD to meet with the Project Officer. Additionally, one meeting shall be conducted each year between NIAID and key personnel involved in the contract (annual meeting). Assume that up to 6 personnel from the contractor will attend this meeting. The annual meeting shall, whenever possible, be combined with the meeting with the expert advisory panel and shall also, if possible be in conjunction with the yearly workshop in a two-day meeting (see NOTE 1 and NOTE 6 TO OFFEROR) and shall be conducted in Bethesda, MD and the contractor's base in alternate years. Back to Item 5 of the Statement of Work.

**NOTE 6 TO OFFEROR:** For the purpose of preparing a cost proposal, assume this workshop will be held in conjunction with the annual contract meeting and shall involve a total of approximately 30-40 persons. Travel costs, including per diem, shall be provided under this contract for the expert advisory panel, key contract personnel (up to 6), as well as 2-4 experts from the TB research field. Back to Item 6 of the Statement of Work.

**NOTE 7 TO OFFEROR:** As approved by the Project Officer, training of qualified outside investigators may be done in the contractor's laboratory and shall include training in all aspects of the model(s). This shall include genetic techniques used to construct mycobacterial strains relevant to the developed models, infection of animals with recombinant mycobacterial strains, and all aspects of characterization of gene function. As part of the proposal, the offeror shall submit a draft training plan. All techniques must include BSL3 training and competency assurance as approved by an appropriate Institutional Biosafety Committee. CDC guidelines for research under BSL3 conditions shall be followed. Back to item 8 of the Statement of Work.

**PART B: NEW ANIMAL MODELS FOR INVASIVE ASPERGILLOSIS**

**NOTE 1 TO OFFEROR:** The establishment of a steering committee to advise the contractor on and help generate and prioritize a research agenda is a critical component of the proposal. The criteria for selection and the final composition of the committee is subject to approval by the Project Officer. This steering committee is to be comprised of a total of 3-6 experts (1-2 of whom may be international researchers) from the field of aspergillosis, mycology, animal model development and fungal genetics. Current animal models of IA are not well characterized with respect to progress of infection and are difficult to conduct. Few labs develop the expertise to employ these models routinely. Therefore input from the scientific community will be crucial for the development of standardized models that will serve as a resource to investigators in IA research. The offeror is **not** to suggest names of individuals for inclusion in the steering committee in the proposal. For the purpose of preparing a cost proposal, assume that travel and per diem will be needed for up to 5 national and 2 international researchers that comprise the steering committee, as well as for 2 personnel from the contractor. Back to item 1 of the Statement of Work.

**NOTE 2 TO OFFEROR:** For the purpose of preparing a cost proposal, assume that travel and per diem will be needed for up to 15 national and 5 international researchers to Bethesda, MD. Back to item 2 of the Statement of Work.

**NOTE 3 TO OFFEROR:** The offeror should, at the time of the proposal, have demonstrable expertise in working with animal models of aspergillosis or other relevant fungal infections. If experience is with other microbial systems, the offeror must address how existing expertise will be extended to research in aspergillosis. For this, the proposal shall contain specific descriptions of the methodologies used to refine the current model of IA. It shall also include at least 2 alternative strategies to quantitative organ culture. For budgeting purposes, model development must include at a minimum both a normal and a neutropenic mouse model as well as another neutropenic model, such as a rabbit or smaller sized animal, that allows for continuous blood sampling. The offeror must submit with the proposal two separate approaches for evaluating target genes in the appropriate model. One of the approaches should incorporate gene profiling studies. Both sets of experiments must include experimental design in brief. The purpose of these described approaches is to demonstrate capability and expertise and does not necessarily constitute the final experiments that will be approved by the Project Officer with input from the expert panel of advisors. For each separate approach, include rationale and one or more supportive experiments with predicted outcome(s). Do not exceed five pages for both approaches combined. The offeror must also have access to

appropriate animal resource facilities for proposed studies and shall provide documentation to this respect in the proposal. Back to Item 3 of the Statement of work.

**NOTE 4 TO OFFEROR:** Models developed under this contract must have the potential to be standardized and widely used to answer key questions in IA infection and disease. To assure agreement within the field of IA, regular consultation with other experts in the field is critical to define parameters of the model that should be standardized. The contractor shall provide detailed standard operating procedures (SOPs) for the utilization of the newly developed model(s) to answer key research questions and hypotheses, as posed by the research community. These SOPs shall include quality control criteria, choice of fungal and animals strains, decision criteria that will be applied to select the best model(s) to evaluate the questions/hypotheses. It shall include procedures for qualified outside investigators to submit questions/hypotheses for evaluation in these newly developed animal models, including design of internet websites, discussions with outside investigators regarding the appropriate choice of models, and what types of reports the contractor will provide to summarize the test findings. Procedures to assure confidentiality of research results must be included. These SOPs are considered deliverables under the contract (see Deliverables and Reporting Requirements). As part of the proposal, the offeror shall submit a draft outlining the above SOPs and shall utilize the proposed model systems as the basis for developing these criteria. This draft will be used in the evaluation of the contract proposal but the procedures outlined in the draft may not be the experiments/procedures that will be approved in the contract. Back to item 4 of the Statement of Work.

**NOTE 5 TO OFFEROR:** As part of this contract, animal models are to be performed for the research community in a timely manner. For this, the contractor is expected to conduct research with the models of IA to answer key scientific questions that are submitted by the research community. Not all parameters may be tested in all models but rather shall involve the most appropriate model(s) to address a specific question. Assume that 2 key personnel will attend a total of one other scientific meeting per year or that 1 key personnel will attend a total of 2 other scientific meetings per year to maintain interactions with the scientific community.Back to item 5 of the Statement of Work.

**NOTE 6 TO OFFEROR:** It is conceivable that new technologies and data will become available during the lifetime of this contract. Therefore, the contractor may propose optimizations or extensions of the models. These optimizations and further research on these models must be negotiated and will be subject to approval by the Project Officer. Back to item 6 of the Statement of Work.

**NOTE 7 TO OFFEROR:** For the purpose of preparing a cost proposal, assume that one or two key personnel will make one visit per year to Bethesda, MD to meet with the project officer and the expert panel. Additionally, one meeting shall be conducted each year between NIAID and key personnel involved in the contract (annual meeting). Assume that up to 6 personnel from the contractor will attend this meeting. The annual meeting shall, whenever possible, be combined with the meeting with the steering committee and shall also, if possible, be in conjunction with the yearly workshop in a two-day meeting (see NOTE 15 and NOTE 8 TO OFFEROR) and shall be conducted in Bethesda, MD and the contractor's base in alternate years. Back to item 7 of the Statement of Work.

**NOTE 8 TO OFFEROR:** For the purpose of preparing a cost proposal, assume this workshop will be held in conjunction with the annual contract meeting and shall involve a total of approximately 30-40 persons. Travel costs, including per diem, shall be provided under this contract for the expert advisory panel, key contract personnel (up to 6), as well as 2-4 experts from the mycology research field. Back to item 8 of the Statement of Work.

**NOTE 9 TO OFFEROR:** As approved by the project officer, training of qualified outside investigators may be done in the contractor's laboratory and shall include training in all aspects of the model(s). This shall include genetic techniques used to construct fungal strains relevant to the developed models, infection of animals with recombinant fungal strains, determination and use of fungal burden and/or surrogate markers for monitoring the infectious process, and all aspects of characterization of gene function. As part of the proposal, the offeror shall submit a draft training plan. All techniques must include appropriate training and competency assurance as approved by an appropriate Institutional Biosafety Committee. CDC guidelines for research under the appropriate BSL conditions shall be followed. Back to item 9 of the Statement of Work.

**Reporting Requirements**
**New Animal Models for TB and Invasive Aspergillosis (IA) Post Genomic Research**
**RFP DMID-03-09**

## REPORTING REQUIREMENTS AND DELIVERABLES

### Part A: New Animal Models for Tuberculosis

Deliverables and Reporting Requirements

The Contractor shall submit to the Contracting Officer and to the Project Officer technical progress reports covering the work accomplished during each reporting period. If the Contractor becomes unable to deliver the reports or other deliverables specified here within the period of performance because of unforeseen difficulties, notwithstanding the exercise of good faith and diligent efforts in performance of the work, the Contractor shall give the Contracting Officer immediate written notice of anticipated delays with reasons.

Technical Reports

In addition to those reports required by the Statement of Work and other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below:

(1) **Quarterly Technical Progress Report** – by the fifteenth working day of the month following the end of each three month period, the Contractor shall submit three (3) copies of a Quarterly Technical Progress Report, comprising two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall include the following specific information:

- a. A cover page that lists the contract number and title, the period of performance being reported, the contractor's names and address, the author(s), and the date of submission;
- b. SECTION I – An introduction covering the purpose, scope of the contract effort and milestones, where applicable, for this period;
- c. SECTION II – A description of overall progress and milestones achieved, where applicable, plus a separate description for each task or other logical segment of work on which effort was expended during the report period. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data for this reporting period. This section should contain a description of any current technical or substantive performance problems encountered, along with proposed corrective action. In addition, the Contractor shall provide a specific listing of the predefined milestone(s), a detailed description of results pertaining to each milestone, and an assessment of the completion of each milestone. For any milestones(s) that may not have been met, the Contractor shall provide an assessment of the feasibility of accomplishing the milestone as well as the additional time or any modifications required. Following completion of the model development period, Section II should also contain a database report of all genes/gene products:
    1. Requested to be tested
    2. Status e.g.
        a. panel decision regarding whether to test
        b. in test including date entered test protocol
        c. completed including date completed
        d. date reported to submitter
    3. Results.
- d. An anticipated work plan for the following six months.
- e. All preprints, reprints, and abstracts referred to in the report shall be submitted along with the report.

Quarterly Technical Progress Reports are not due for periods in which an annual or final report is due.

(2) **Annual Reports** – On the anniversary date of the contract, the Contractor shall submit three (3) copies of an Annual Technical Progress Report comprising two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall detail, document, and summarize the results of the entire contract work for the period covered and shall include a summary of data accumulated to date. These reports shall be in sufficient detail to comprehensively explain the results achieved. A summary of work proposed for the next reporting period should also be included in the report. An annual report will not be required for the period

when the final report is due. Preprints and reprints of papers and abstracts not submitted in the quarterly report shall be submitted.

(3) **Status Report** – Within three months after the end of the development phase (24 months) of award of this contract, the Contractor shall submit three (3) copies of a comprehensive status report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. On the basis of progress completed during this time, the Government intends to make an assessment of progress towards the predefined milestones. This one time report shall outline the composition of all genetic engineering protocols and all developed models, provide detailed standardized procedures for their implementation (SOP's), including genetic engineering protocols and all quality control measures and shall include a plan for how the contractor will perform these models as a service to the community. This plan will address: procedures for receiving and prioritizing genes/gene products submitted by qualified investigators, including the contractor;

1. procedures for interaction with the community to solicit gene submissions for testing;
2. what types of information will be required from the outside investigator to allow rapid evaluation of the submitted genes in the animal model(s);
3. decision criteria for selection of various models on the basis of what is known about a submitted gene.

(4) **Final Report** – By the completion date of the contract, the Contractor shall submit three (3) copies of a comprehensive Final Report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. This report will provide a summary of the results of the entire contract work for the complete performance period. This report will be in sufficient detail to comprehensively explain the results achieved and will be submitted no later than the completion date of the contract.

The final report shall contain:

1. A cover page as describe above.
2. An introduction covering the purpose and scope of the contract effort.
3. A description of the overall progress, plus a separate description of the final status of each gene/gene product addressed under the contract and all subcontracts. Descriptions will include detailed information on significant results achieved, as well as any technology developed or improved, together with pertinent data.
4. A discussion of the contractor's plan for further development of any products.
5. Copies of any abstracts, manuscripts, publications.
6. Copies of any patents filed or granted to the Contractor for work performed during the course of this award.

Transition Report

Six months prior to the expiration date of this contract, the Contractor shall submit three (3) copies of a Transition Report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. This report shall outline the composition of all genetic engineering protocols and all developed models, provide detailed standardized procedures for their implementation (SOP's), including genetic engineering protocols and all quality control measures. This report shall also include a plan for transfer of intellectual and tangible property to third parties or the NIH in a manner that would permit third party companies or non-governmental organizations to utilize the model(s) or continue assessment of previously submitted genes/gene products.

**Report Format**: All reports shall contain a title page, which includes:

(1) Contract number and title
(2) Type of report (Quarterly, Annual, Status, Final or Transition)
(3) Period of performance being reported
(4) Contractor's name and address
(5) Author(s)
(6) Date of submission

1. Technical Progress Reports

| Item # | Type of Deliverable | Description | Initial Report Due | Subsequent Reports Due |
|---|---|---|---|---|
| 1. | Quarterly Technical Report | Outlined above. | Three months after Award date | The 15th of the month following each reporting period. |
| 2. | Annual Technical | Outlined above. | One year after | Annually |

| | | | |
|---|---|---|---|
| | Report | | Award date. |
| 3. | Status Report | Outlined above. | Between 24 and 27 months of Award date as a **one-time** report. |
| 4. | Final Report | Outlined above. | On or before the completion date of the Contract. |

2. Other Deliverables:

| Item # | Type of Deliverable | Description | Report Due |
|---|---|---|---|
| 5. | Transition Report | Outlined above. | Six months before Contract expiration date. |

**Part B: New Animal Models for Invasive Aspergillosis (IA)**

Deliverables and Reporting Requirements

The Contractor shall submit to the Contracting Officer and to the Project Officer technical progress reports covering the work accomplished during each reporting period. If the Contractor becomes unable to deliver the reports or other deliverables specified here within the period of performance because of unforeseen difficulties, notwithstanding the exercise of good faith and diligent efforts in performance of the work, the Contractor shall give the Contracting Officer immediate written notice of anticipated delays with reasons.

Technical Reports

In addition to those reports required by the Statement of Work and other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below:

(5) **Quarterly Technical Progress Report** – by the fifteenth working day of the month following the end of each three month period, the Contractor shall submit three (3) copies of a Quarterly Technical Progress Report, comprising two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall include the following specific information:

- a. A cover page that lists the contract number and title, the period of performance being reported, the contractor's names and address, the author(s), and the date of submission;
- b. SECTION I – An introduction covering the purpose, scope of the contract effort and milestones, where applicable, for this period;
- c. SECTION II – A description of overall progress and milestones achieved, where applicable, plus a separate description for each task or other logical segment of work on which effort was expended during the report period. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data for this reporting period. This section should contain a description of any current technical or substantive performance problems encountered, along with proposed corrective action. In addition, the Contractor shall provide a specific listing of the predefined milestone(s), a detailed description of results pertaining to each milestone, and an assessment of the completion of each milestone. For any milestones(s) that may not have been met, the Contractor shall provide an assessment of the feasibility of accomplishing the milestone as well as the additional time or any modifications required. Following completion of the model development period, Section II should also contain a database report of all scientific questions:
    1. Requested to be tested
    2. Status e.g.
        a. panel decision regarding whether to test
        b. in test including date entered test protocol and which model(s)
        c. completed including date completed
        d. date reported to submitter
    3. Results.
- d. An anticipated work plan for the following six months.
- e. All preprints, reprints, and abstracts referred to in the report shall be submitted along with the report.

Quarterly Technical Progress Reports are not due for periods in which an annual or final report is due.

(6) **Annual Reports** – On the anniversary date of the contract, the Contractor shall submit three (3) copies of an Annual Technical Progress Report comprising two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall detail, document, and summarize the results of the entire contract work for the period covered and shall include a summary of data accumulated to date. These reports shall be in sufficient detail to comprehensively explain the results achieved. A summary of work proposed for the next reporting period should also be included in the report. An annual report will not be required for the period when the final report is due. Preprints and reprints of papers and abstracts not submitted in the quarterly report shall be submitted.

(7) **Status Report** – Within three months after the end of the development phase (36 months) of award of this contract, the Contractor shall submit three (3) copies of a comprehensive status report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. On the basis of progress completed during this time, the Government intends to make an assessment of progress towards the predefined milestones. This one time report shall outline the composition of all developed models, provide detailed standardized procedures for their implementation (SOP's), including genetic engineering protocols and all quality control measures and

shall include a plan for how the contractor will perform these models as a service to the community. This plan will address:

1. how best to identify unanswered scientific questions and establish research priorities based on public health need, scientific opportunities and advances in aspergillosis research;
2. interactions with the steering committee and the scientific community to identify further research gaps and provide a prioritized agenda;
3. procedures for receiving and prioritizing research questions submitted by qualified investigators, including the contractor, to be addressed with the models developed under this contract;
4. procedures for interaction with the community to solicit input for the research agenda and provide hypotheses for evaluation in the newly adapted animal models;
5. decision criteria for selection of various models to answer specific research questions (i.e. role of specific genes in fungal virulence and host-pathogen interaction).

(8) **Final Report** – By the completion date of the contract, the Contractor shall submit three (3) copies of a comprehensive Final Report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. This report will provide a summary of the results of the entire contract work for the complete performance period. This report will be in sufficient detail to comprehensively explain the results achieved and will be submitted no later than the completion date of the contract.

The final report shall contain:

1. A cover page as describe above.
2. An introduction covering the purpose and scope of the contract effort.
3. A description of the overall progress, plus a separate description of the final status of each gene/gene product addressed under the contract and all subcontracts. Descriptions will include detailed information on significant results achieved, as well as any technology developed or improved, together with pertinent data.
4. A discussion of the contractor's plan for further development of any products.
5. Copies of any abstracts, manuscripts, publications.
6. Copies of any patents filed or granted to the Contractor for work performed during the course of this award.

Transition Report

Six months prior to the expiration date of this contract, the Contractor shall submit three (3) copies of a Transition Report, two (2) copies to the Project Officer and one (1) copy to the Contracting Officer. This report shall outline the composition of all genetic engineering protocols and all developed models, provide detailed standardized procedures for their implementation (SOP's), including genetic engineering protocols and all quality control measures. This report shall also include a plan for transfer of intellectual and tangible property to third parties or the NIH in a manner that would permit third party companies or non-governmental organizations to utilize the model(s) or continue assessment of previously submitted scientific questions.

**Report Format**: All reports shall contain a title page, which includes:

(1) Contract number and title
(2) Type of report (Quarterly, Annual, Status, Final or Transition)
(3) Period of performance being reported
(4) Contractor's name and address
(5) Author(s)
(6) Date of submission

1. Technical Progress Reports

| Item # | Type of Deliverable | Description | Initial Report Due | Subsequent Reports Due |
|---|---|---|---|---|
| 1. | Quarterly Technical Report | Outlined above. | Three months after Award date | The 15th of the month following each reporting period. |
| 2. | Annual Technical Report | Outlined above. | One year after Award date. | Annually |
| 3. | Status Report | Outlined above. | Between 24 and 27 months of Award date as a **one-time** report. | |

| | | | |
|---|---|---|---|
| 4. | Final Report | Outlined above. | On or before the completion date of the Contract. |

2. Other Deliverables:

| Item # | Type of Deliverable | Description | Report Due |
|---|---|---|---|
| 5. | Transition Report | Outlined above. | Six months before Contract expiration date. |

## SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

**A Sample Uniform Contract Format may be found at the following website:**

http://www4.od.nih.gov/ocm/contracts/rfps/sampkt.htm

**[Disregard SECTION I and J of this sample. Those SECTIONS have been incorporated as part of this RFP.]**

## SECTION I - CONTRACT CLAUSES

**THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.**

**BECAUSE THIS IS A STREAMLINED RFP, ARTICLES I.2. AND I.3., WHICH IDENTIFY ANY AUTHORIZED ADDITIONS, SUBSTITUTIONS AND/OR MODIFICATIONS TO THE GENERAL CLAUSES, WILL BE BASED ON THE TYPE OF CONTRACT/CONTRACTOR AND WILL BE DETERMINED DURING NEGOTIATIONS.**

**ARTICLE I.1. GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)**

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at this URL: http://www.arnet.gov/far/.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CHAPTER 1) CLAUSES

| FAR Clause No. | Date | Title |
|---|---|---|
| 52.202-1 | Dec 2001 | Definitions |
| 52.203-3 | Apr 1984 | Gratuities (Over $100,000) |
| 52.203-5 | Apr 1984 | Covenant Against Contingent Fees (Over $100,000) |
| 52.203-6 | Jul 1995 | Covenant Against Contingent Fees (Over $100,000) |
| 52.203-7 | Jul 1995 | Anti-Kickback Procedures (Over $100,000) |
| 52.203-8 | Jan 1997 | Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity (Over $100,000) |
| 52.203-10 | Jan 1997 | Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000) |
| 52.203-12 | Jun 1997 | Limitation on Payments to Influence Certain Federal Transactions (Over $100,000) |
| 52.204-4 | Aug 2000 | Printing/Copying Double-Sided on Recycled Paper (Over $100,000) |
| 52.209-6 | Jul 1995 | Protecting the Governments Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000) |
| 52.215-2 | Jun 1999 | Audit and Records - Negotiation (Over $100,000) |
| 52.215-8 | Oct 1997 | Order of Precedence – Uniform Contract Format |
| 52.215-10 | Oct 1997 | Price Reduction for Defective Cost or Pricing Data |
| 52.215-12 | Oct 1997 | Subcontractor Cost or Pricing Data (Over $500,000) |
| 52.215-14 | Oct 1997 | Integrity of Unit Prices (Over $100,000) |
| 52.215-15 | Dec 1998 | Pension Adjustments and Asset Reversions |
| 52.215-18 | Oct 1997 | Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) Other Than Pensions |
| 52.215-19 | Oct 1997 | Notification of Ownership Changes |
| 52.215-21 | Oct 1997 | Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data - Modifications |
| 52.216-7 | Feb 2002 | Allowable Cost and Payment |
| 52.216-8 | Mar 1997 | Fixed Fee |
| 52.219-8 | Oct 2000 | Utilization of Small Business Concerns (Over $100,000) |
| 52.219-9 | Jan 2002 | Small Business Subcontracting Plan (Over $500,000) |

| | | |
|---|---|---|
| 52.219-16 | Jan 1999 | Liquidated Damages - Subcontracting Plan (Over $500,000) |
| 52.222-2 | Jul 1990 | Payment for Overtime Premium (Over $100,000) (NOTE: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.) |
| 52.222-3 | Aug 1996 | Convict Labor |
| 52.222-26 | Feb 1999 | Equal Opportunity |
| 52.222-35 | Dec 2001 | Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans |
| 52.222-36 | Jun 1998 | Affirmative Action for Workers with Disabilities |
| 52.222-37 | Dec 2001 | Employment Reports on Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans |
| 52.223-6 | May 2001 | Drug-Free Workplace |
| 52.223-14 | Oct 2000 | Toxic Chemical Release Reporting |
| 52.225-1 | Feb 2002 | Buy American Act - Balance of Payments Program – Supplies |
| 52.225-13 | Jul 2000 | Restrictions on Certain Foreign Purchases |
| 52.227-1 | Jul 1995 | Authorization and Consent, Alternate I (Apr 1984) |
| 52.227-2 | Aug 1996 | Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000) |
| 52.227-11 | Jun 1997 | Patent Rights - Retention by the Contractor (Short Form) (NOTE: In accordance with FAR 27.303 (a) (2), paragraph (f) is modified to include the requirements in FAR 27.303 (a) (2) (i) through (iv). The frequency of reporting in (i) is annual. |
| 52.227-14 | Jun 1987 | Rights in Data – General |
| 52-232-9 | Apr 1984 | Limitation on Withholding of Payments |
| 52.232-17 | Jun 1996 | Interest (Over $100,000) |
| 52.232-20 | Apr 1984 | Limitation of Cost |
| 52.232-23 | Jan 1986 | Assignment of Claims |
| 52.232-25 | Feb 2002 | Prompt Payment |
| 52.232-34 | May 1999 | Payment by Electronic Funds Transfer--Other Than Central Contractor Registration |
| 52.233-1 | Dec 1998 | Disputes |
| 52.233-3 | Aug 1996 | Protest After Award |
| 52.242-1 | Apr 1984 | Notice of Intent to Disallow Costs |
| 52.242-3 | May 2001 | Penalties for Unallowable Costs (Over $500,000) |
| 52.242-4 | Jan 1997 | Certification of Final Indirect Costs |
| 52.242-13 | Jul 1995 | Bankruptcy (Over $100,000) |

| | | |
|---|---|---|
| 52.243-2 | Aug 1987 | Changes - Cost Reimbursement, Alternate V (Apr 1984) |
| 52.244-2 | Aug 1998 | Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B., Advance Understandings. |
| 52.244-5 | Dec 1996 | Competition in Subcontracting (Over $100,000) |
| 52.245-5 | Jan 1986 | Government Property (Cost-Reimbursement, Time and Material, or Labor Hour Contract) |
| 52.246-23 | Feb 1997 | Limitation of Liability (Over $100,000) |
| 52.249-6 | Sep 1996 | Termination (Cost-Reimbursement) |
| 52.249-14 | Apr 1984 | Excusable Delays |

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES

| HHSAR Clause No. | Date | Title |
|---|---|---|
| 352.202-1 | Jan 2001 | Definitions - with Alternate paragraph (h) (Jan 2001) |
| 352.228-7 | Dec 1991 | Insurance - Liability to Third Persons |
| 352.232-9 | Apr 1984 | Withholding of Contract Payments |
| 352.233-70 | Apr 1984 | Litigation and Claims |
| 352.242-71 | Apr 1984 | Final Decisions on Audit Findings |
| 352.270-5 | Apr 1984 | Key Personnel |
| 352.270-6 | Jul 1991 | Publication and Publicity |

[END OF GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – Rev. 02/2002]

## SECTION J - LIST OF ATTACHMENTS

The following Attachments are provided in full text with this Solicitation:

**PROPOSED DEVIATIONS TO REQUIRED GENERAL CONTRACT CLAUSES FAR 52.227-11 AND FAR 52.227-14 (Attached to this listing)**

**PACKAGING AND DELIVERY OF PROPOSALS (Attached to this listing)**

**HOW TO PREPARE AN ELECTRONIC PROPOSAL: (Attached to this listing)**

**PROPOSAL INTENT RESPONSE SHEET [SUBMIT ON/BEFORE: July 1, 2002 (Attached to this listing)**

[NOTE: Your attention is directed to the "Proposal Intent Response Sheet". If you intend to submit a proposal, you must complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMB's coordination of the electronic submission and review of proposals.]

**RFP FORMS AND ATTACHMENTS:**

THE RFP FORMS/ATTACHMENTS LISTED BELOW ARE AVAILABLE IN A VARIETY OF FORMATS AND MAY BE VIEWED OR DOWNLOADED DIRECTLY FROM THIS SITE:

http://www.niaid.nih.gov/contract/ref.htm

**APPLICABLE TO TECHNICAL PROPOSAL (INCLUDE THESE DOCUMENTS/FORMS WITH YOUR TECHNICAL PROPOSAL):**

- **Technical Proposal Cover Sheet**
- **Summary of Related Activities**

**APPLICABLE TO BUSINESS PROPOSAL (INCLUDE WITH YOUR BUSINESS PROPOSAL):**

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan Format *[if applicable]***
- **Breakdown of Proposed Estimated Cost (plus fee) and Labor Hours**
- **Offeror's Points of Contact**

**TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):**

- **NIH(RC)-1: Invoice/Financing Request Instructions for NIH Cost-Reimbursement Type Contracts**
- **NIH-2706: Financial Report of Individual Project Contract**
- **Instructions for Completing Form NIH-2706**
- **NIH(RC)-7: Procurement of Certain Equipment, (OMB Bulletin 81-16)**
- **Safety and Health, HHSAR Clause 352.223-70**

# PROPOSED DEVIATIONS TO REQUIRED GENERAL CONTRACT CLAUSES FAR 52.227-11 AND FAR 52.227-14

These planned contracts represent one segment of the Post-genomic Development Program in Tuberculosis (TB) and Mycology within the Division of Microbiology and Infectious Diseases (DMID), NIAID. This project complements efforts in genome research and model development that are an integral element of NIAID's mission to further basic research in the biology of the microbe, host pathogen interaction and pathology to result in the development of improved vaccine- drug and diagnostic candidates for use in TB and Invasive Aspergillosis (IA). This project is intended to develop and ultimately provide animal model resources to the research community to help translate data ensuing from genomic research into putative candidates for novel preventive and therapeutic strategies. As such, this project is divided into two separate aspects, Part-A dealing with research pertaining to TB, and Part-B pertaining to research in IA. This project first seeks to develop models and research methodologies, and then to make these models and methodologies available to researchers under the contract to enable the in *vivo* validation of putative target genes in a relatively rapid throughput manner, allowing the creation of biological information critical to secure intellectual property claims. The ability to assess biological function of putative target genes in a relatively short time frame while maintaining intellectual property rights to any data ensuing from these evaluations would allow investigators protection of claims as to the suitability of these genes as targets for vaccine and drug development, as well as diagnostics and possibly novel enabling technologies.

Both parts of this contract will develop animal models suitable to answer critical questions in TB or IA research, and will make these models available for the evaluation of biological function of putative gene products. By providing information on biological activity developed under these contracts to suppliers of candidate genes, the NIAID seeks to stimulate research and development in all sectors of the scientific community.

Because the goal of this NIAID post genomic animal model program is to promote the determination of critical biological information, it will be necessary to restrict certain rights of the contractor providing animal model testing to either attract suppliers of proprietary compositions or enable NIAID to offer a package of intellectual property rights to a collaborator for commercialization. It is anticipated that the great majority of genes and ideas submitted to the NIAID for testing will be proprietary in nature, and our experience has demonstrated that suppliers are reluctant to provide new compositions or ideas without complete assurance that their intellectual property rights are protected. In addition to the need to protect third party suppliers' proprietary rights, it is also necessary to consolidate into a single package the intellectual property rights that may arise in the performance of multiple contracts within this NIAID program.

Thus, the NIAID intends to seek a deviation from FAR clause 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989). Pursuant to a Determination of Exceptional Circumstances (DEC) as required by FAR 27.303, the clause at FAR 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989) will be modified to restrict the contractor's rights to subject inventions arising under the contract. Specifically, the contractor will be required to assign to the Government or, if deemed appropriate by the NIAID and subject to certain rights reserved to the Government, to a collaborating party designated by the Government the entire right, title and interest throughout the world to each subject invention, except to the extent that rights are retained by the Contractor under the Greater Rights Determination provision of the clause. The contractor may request greater rights to an identified invention, and the NIH will consider whether granting the requested rights will interfere with rights of the Government or any collaborating party or otherwise impede the ability of the Government or others to develop new candidates for therapies, disease prevention and diagnosis as well as potential enabling technologies that may result from data ensuing from evaluations performed under this contract useful for TB and IA. Contractors are encouraged to request greater rights where inventions relate to technology outside NIAID's program and where the contractor has negotiated with a supplier of a proprietary composition for the disposition of patent rights concerning a subject invention related to the composition.

Furthermore, in order to protect the intellectual property rights of third party suppliers, the timing of data publicationwill need to be restricted to allow adequate time for patent applications to be filed on inventions arising from the contracts. This would be accomplished by a deviation from FAR clause 52.227-14, Rights in Data-General (June 1987). Specifically, although NIAID encourages the publication of articles on research results, FAR 52.227-14 Rights in Data-General (June 1987) will be narrowly modified to restrict the Contractor's right to use, release to others, reproduce, distribute, and publish data produced or used by the contractor in the performance of this contract in order to protect the supplier's proprietary rights, to protect data that will be submitted as part of a regulatory filing, and to delay the publication of data as necessary to obtain patent protection. NIAID will reserve the right to coordinate the timing of data publication with the supplier so that appropriate domestic and international invention applications may be filed. In general, a reasonable delay in publishing is expected to be less than six months.

PACKAGING/DELIVERY/ELECTRONIC SUBMISSION OF THE PROPOSAL

*Listed below are delivery instructions for the submission of both PAPER and ELECTRONIC COPIES of your proposal.*

*PAPER SUBMISSION:* The paper copy is the official copy for recording timely receipt of proposals. *You are required to submit one original paper copy of your proposal along with the number of extra copies required below.*

*ELECTRONIC SUBMISSION: In addition to the paper submission, you are required to submit your proposal electronically through the CRON (Contracts Review Online) in accordance with the instructions provided below. If you experience difficulty or are unable to transmit, you should submit your proposal on a CD-Rom or ZipDisk by an express delivery service. We can then upload your proposal into the electronic system. You must certify that both the original paper and electronic versions of the proposal are identical.*

*SUBMISSION OF PROPOSALS BY FACSIMILE IS NOT ACCEPTABLE.*

## Shipment and marking of paper copies shall be as indicated below:

### A. EXTERNAL PACKAGE MARKING:

In addition to the address cited below, mark each package as follows:

"RFP-NIH-NIAID-DMID-03-09
TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

### B. NUMBER OF COPIES:

The number of copies required of each part of your proposal are as specified below.

**Technical Proposal:** One (1) unbound signed original and five (5) unbound copies. Ten (10) copies of all material not available electronically (i.e. SOPs, Pertinent Manuals, Nonscannable Figures or Data, and Letters of Collaboration/Intent).

**Business Proposal:** One (1) unbound signed original and 5 unbound copies.

### C. PAPER COPIES and CD-Rom or ZipDisk to:

| If Hand Delivery or Express Service | If using U.S. Postal Service |
|---|---|
| Ross Kelley<br>Contracting Officer<br>Contract Management Branch, DEA<br>NIAID, NIH<br>6700-B Rockledge Drive, Room 2230<br>Bethesda, Maryland 20817 | Ross Kelley<br>Contracting Officer<br>Contract Management Branch, DEA<br>NIAID, NIH<br>6700-B Rockledge Drive, Room 2230, MSC 7612<br>Bethesda, Maryland 20892-7612 |

*NOTE: All material sent to this office by Federal Express should be sent to the Hand Carried Address.*

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered (20817 zip code) address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance with HHSAR 352.215-70, Late Proposals and Revisions (NOV 1986).

# HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

**PAGE LIMITS -- THE TECHNICAL PROPOSAL IS LIMITED TO NOT-TO-EXCEED 200 PAGES for Part A and 200 Pages for Part B** [INCLUDING: Appendices, Attachments, Operating Manuals, Non-Scannable Figures or Data, Letters of Intent, etc.]. ANY PORTIONS OF YOUR PROPOSAL NOT AVAILABLE ELECTRONICALLY ARE ALSO CONSIDERED TO BE INCLUDED IN THE TOTAL PAGE LIMITATION. PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND WILL NOT BE READ OR EVALUATED.

**Note that although no page limit has been placed on the Business Proposal, offerors are encouraged to limit its content to only those documents necessary to provide adequate support for the proposed costs.**

**ELECTRONIC SUBMISSION** – To submit a proposal electronically under this RFP, offerors will need to prepare the proposal on a word processor or spreadsheet program (for the business portion) and convert them to Adobe Acrobat Portable Document Format (.pdf). THE TECHNICAL PROPOSAL AND BUSINESS PROPOSAL MUST BE CONTAINED ON SEPARATE FILES which must be identified as either TECHNICAL or BUSINESS and include some recognizable portion of the ORGANIZATION NAME.

Please note that the electronic submission does not replace the requirement to submit a signed, unbound original paper copy of both your Technical and Business Proposal, along with any required unbound duplicate copies. These paper originals should be mailed or hand-delivered to the address provided in this attachment and must be received on/before the closing date and time.

There is no limit to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined above. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 4.0 (or higher).

**Formatting Requirements:**

- Do not embed sound or video (e.g., MPEG) files into the proposal documents. The evaluation system does not have the capability to read these files.
- Keep graphics embedded in documents as simple as possible. Complex graphics require longer periods for the computers used in the evaluation system to draw, and redraw these figures and scrolling through the document is slowed significantly.
- Type density and size must be 10 to 12 points. If constant spacing is used, there should be no more than 15 cpi, whereas proportional spacing should provide an average of no more than 15 cpi. There must be no more than six lines of text within a vertical inch. Margins must be set to 1 inch around.
- Paper size should not exceed 8-1/2 x 11. Larger paper sizes will be counted as 2 pages.
- Limit colors to 256 colors at 1024 x 768 resolution; avoid color gradients.
- Simplify the color palette used in creating figures.
- Be aware of how large these graphics files become. Large files are discouraged.
- Limit scanned images as much as possible.
- Limit appendices and attachments to relevant technical proposal information (e.g., SOPs, pertinent manuals, non-scannable figures or data, resumes, letters of commitment/intent).

**SUBMISSION OF "PROPOSAL INTENT TO RESPOND SHEET":**

Approximately TWO weeks prior to the due date of the proposals, all offerors who submitted a "Proposal Intent Response Sheet" will be provided with specific electronic access information and electronic proposal transmission instructions. For this reason, it is imperative that all offerors who are intending to submit a proposal in response to this RFP contact the Contract Specialist identified in this RFP and complete and submit the attached "Proposal Intent Response Sheet" by the date provided on that Attachment.

**CREATE ADOBE PDF ONLINE** -- Adobe will allow you to create 5 documents on a trial for free. If you want to use the site regularly it costs $10/month or $100/year. Please link to the following URL for information:

https://createpdf.adobe.com/index.pl/3847995518.39272?BP=IE

**LOG-IN / TRANSMISSION INSTRUCTIONS:**

1. Log-in Site: Will be provided by the Contract Specialist after receipt of the "Proposal Intent Response Sheet"
2. Log-in Name: Will be provided by the Contract Specialist.
3. Log-in Password: Will be provided via telephone by the Contract Specialist after Log-in Name is provided.

4. Procedure -- When your proposal is completed and converted to a PDF file using Adobe Acrobat, it is ready to be transmitted electronically. You must upload separate Technical and Business Proposal Files. It is recommended that proposals be transmitted a few days before the due date so that you will have sufficient time to overcome any transmission difficulties.

- You must have Explorer 3.1 or higher.
- It is essential that you use antiviral software to scan all documents.
- Click on "Sign On" and enter your log-in name and password.
- Click on "Browse" to locate your saved files on your computer.
- Click on "Upload Proposal" after you have located the correct file.
- After a file is uploaded, a link to the file will appear under "Upload Files" at the bottom of the screen. Click on that link to view the uploaded file.
- If you experience difficulty in accessing your documents, please contact the appropriate NIH contracts office immediately.
- If you wish to revise your proposal before the closing date and time, simply log in again and re-post.

**USER ACCESS TO THE POSTING SITE WILL BE DENIED AFTER THE RFP CLOSING DATE AND TIME PROVIDED WITH THIS RFP OR ITS MOST RECENT AMENDMENT(S).**

# PROPOSAL INTENT RESPONSE SHEET

**RFP No.:** NIH-NIAID-DMID-03-09 Part A
**RFP Title:** New Animal Models for Tuberculosis (TB)

Please review the attached Request for Proposal. Furnish the information requested below and return this page by 7/12/2002. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

**Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.**

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

**Company/Institution Name (print):** _____
**Address (print):** _____
_____
_____
_____

**Project Director's Name (print):** _____
**Title (print):** _____
**Signature/Date:** _____
**Telephone Number and E-mail Address (print clearly):**
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

**Name:** _____
**Title:** _____
**E-Mail Address:** _____
**Telephone Number:** _____

**Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):**
_____
_____
_____
_____
*(Continue list on a separate page if necessary)*

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Ross Kelley
RFP-NIH-NIAID- 03-09 Part A
FAX# (301) 402-2234
Email : rk17a@nih.gov

# PROPOSAL INTENT RESPONSE SHEET

**RFP No.:** NIH-NIAID-DMID-03-09 Part B
**RFP Title:** New Models for Invasive Aspergillosis (IA)
Please review the attached Request for Proposal. Furnish the information requested below and return this page by 7/12/2002. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

**Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.**

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

**Company/Institution Name (print):** _____
**Address (print):** _____
_____
_____
_____

**Project Director's Name (print):** _____
**Title (print):** _____
**Signature/Date:** _____
**Telephone Number and E-mail Address (print clearly):**
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

**Name:** _____
**Title:** _____
**E-Mail Address:** _____
**Telephone Number:** _____

**Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):**
_____
_____
_____
_____
*(Continue list on a separate page if necessary)*

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn:
RFP-NIH-NIAID-DMID-03-09 PART B
FAX# (301) 402-2234
Email : rk17a@nih.gov

# PROPOSAL INTENT RESPONSE SHEET

**RFP No.:** NIH-NIAID-DMID-03-09 Part B
**RFP Title:** New Animal Models For Invasive Aspergillosis (IA)

Please review the attached Request for Proposal. Furnish the information requested below and return this page by _____. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

**Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.**

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

**Company/Institution Name (print):** _____
**Address (print):** _____
_____
_____
_____

**Project Director's Name (print):** _____
**Title (print):** _____
**Signature/Date:** _____
**Telephone Number and E-mail Address (print clearly):**
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

**Name:** _____
**Title:** _____
**E-Mail Address:** _____
**Telephone Number:** _____

**Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):**
_____
_____
_____
_____
*(Continue list on a separate page if necessary)*

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn:
RFP-NIH-NIAID-
FAX# (301)
Email :

# SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

**Representations, Certifications, and Other Statements of Offerors or Quoters (Negotiated).**

1. REPRESENTATIONS AND CERTIFICATIONS

The Representations and Certifications required by this particular acquisition can be accessed electronically from the INTERNET at the following address:

http://rcb.nci.nih.gov/forms/rcneg.pdf

If you are unable to access this document electronically, you may request a copy from the Contracting Officer identified on the cover page of this solicitation.

**IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT THEM AS PART OF YOUR BUSINESS PROPOSAL.**

# SECTION L - INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

**1.** GENERAL INFORMATION

a. **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the offeror in preparing its Representations and Certifications (See Section K of this RFP), specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(1) The North American Industry Classification System (NAICS) code for this acquisition is 54171.
(2) The small business size standard is 500 employees.

b. **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that two awards will be made from this solicitation (one for Part A and one for Part B) and that the award(s) will be made on/about May 5, 2003.

It is anticipated that the awards from this solicitation will be a multiple-year Cost Reimbursement type Completion contracts with a Period of Performance of seven years, and that incremental funding will be used [see Section L.2.c. Business Proposal Instructions].

c. **ESTIMATE OF EFFORT**

Part A:

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately 120,848 labor hours for all seven years. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

Part B:
It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately 74,256 labor hours for all seven years. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

d. **COMMITMENT OF PUBLIC FUNDS**

The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public funds in connection with the proposed procurement. Any other commitment, either explicit or implied, is invalid.

e. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

Offerors shall direct all communications to the attention of the Contract Specialist or Contracting Officer cited on the face page of this RFP. Communications with other officials may compromise the competitiveness of this acquisition and result in cancellation of the requirement.

f. **RELEASE OF INFORMATION**

Contract selection and award information will be disclosed to offerors in accordance with regulations applicable to negotiated acquisition. Prompt written notice will be given to unsuccessful offerors as they are eliminated from the competition, and to all offerors following award.

g. **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are [significantly more important than cost or price/approximately equal to cost or price/significantly less important than cost or price]. The relative importance of the evaluation factors is specified in SECTION M of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

h. **PREPARATION COSTS**

This RFP does not commit the Government to pay for the preparation and submission of a proposal.

i. **SERVICE OF PROTEST** (AUGUST 1996) - FAR 52.233-2

(a) Protests, as defined in section 33.101 of the Federal Acquisition Regulation, that are filed directly with an agency, and copies of any protests that are filed with the General Accounting Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Brenda J. Velez
Contracting Officer
Contract Management Branch, DEA
National Institute of Allergy and Infectious Diseases
6700-B Rockledge Drive, Room 2230, MSC 7612
BETHESDA MD 20892-7612

(b) The copy of any protest shall be received in the office designated above within one day of filing a protest with the GAO.

(End of Provision)

j. **LATE PROPOSALS AND REVISIONS**, HHSAR 352.215-70

Notwithstanding the procedures contained in FAR 52.215-1(c)(3) of the provision of this solicitation entitled Instructions to Offerors—Competitive Acquisition, a proposal received after the date specified for receipt may be considered if it offers significant cost or technical advantages to the Government; and it was received before proposals were distributed for evaluation, or within five calendar days after the exact time specified for receipt, whichever is earlier.

(End of provision)

## GENERAL INSTRUCTIONS

### INTRODUCTION

The following instructions will establish the acceptable minimum requirements for the format and contents of proposals. Special attention is directed to the requirements for technical and business proposals to be submitted in accordance with these instructions.

### Contract Type and General Clauses

It is contemplated that a cost-reimbursement completion type contract will be awarded. (See General Information) Any resultant contract shall include the clauses applicable to the selected offeror's organization and type of contract awarded as required by Public Law, Executive Order, or acquisition regulations in effect at the time of execution of the proposed contract.

### (1) Authorized Official and Submission of Proposal

The proposal must be signed by an official authorized to bind your organization and must stipulate that it is predicated upon all the terms and conditions of this RFP. Your proposal shall be submitted in the number of copies, to the addressees, and marked as indicated in the Attachment entitled, PACKAGING AND DELIVERY OF PROPOSAL, Part III, Section J hereof. Proposals will be typewritten, paginated, reproduced on letter size paper and will be legible in all required copies. To expedite the proposal evaluation, all documents required for responding to the RFP should be placed in the following order:

I. COVER PAGE

Include RFP title, number, name of organization, identification of the proposal part, and indicate whether the proposal is an original or a copy.

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions and as specified in SECTION J, List of Attachments.

III. BUSINESS PROPOSAL

It is recommended that the business proposal consist of a cover page, a table of contents, and the information requested in the Business Proposal Instructions and as specified in SECTION J, List of Attachments.

### (2) Proposal Summary and Data Record (NIH-2043)

The Offeror must complete the Form NIH-2043, attached, with particular attention to the length of time the proposal is firm and the designation of those personnel authorized to conduct negotiations. (See Section J, Attachment entitled, PROPOSAL SUMMARY AND DATA RECORD).

### (3) Separation of Technical and Business Proposals

The proposal must be prepared in two parts: a "Technical Proposal" and a "Business Proposal." Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal must include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the offeror's understanding of the project may be evaluated (See Attachment entitled, TECHNICAL PROPOSAL COST INFORMATION/SUMMARY OF LABOR AND DIRECT COSTS).) However, the technical proposal should **not** include pricing data relating to individual salary information, indirect cost rates or

amounts, fee amounts (if any)., and total costs. The technical proposal should disclose your technical approach in as much detail as possible, including, but not limited to, the requirements of the technical proposal instructions.

(4) **Alternate Proposals**

You may, at your discretion, submit alternate proposals, or proposals which deviate from the requirements; provided, that you also submit a proposal for performance of the work as specified in the statement of work. Such proposals may be considered if overall performance would be improved or not compromised and if they are in the best interests of the Government. Alternative proposals, or deviations from any requirements of this RFP, shall be clearly identified.

(5) **Evaluation of Proposals**

The Government will evaluate technical proposals in accordance with the criteria set forth in PART IV, SECTION M of this RFP.

(6) **Potential Award Without Discussions**

The Government reserves the right to award a contract without discussions if the Contracting Officer determines that the initial prices are fair and reasonable and that discussions are not necessary.

(7) **Use of the Metric System of Measurement**

It is the policy of the Department of Health and Human Services to support the Federal transition to the metric system and to use the metric system of measurement in all procurements, grants, and other business related activities unless such use is impracticable or is likely to cause significant inefficiencies.

The offeror is encouraged to prepare their proposal using either "Hard Metric," "Soft Metric," or "Dual Systems" of measurement. The following definitions are provided for your information:

**Hard Metric** - The replacement of a standard inch-pound size with an accepted metric size for a particular purpose. An example of size substitution might be: selling or packaging liquids by the liter instead of by the pint or quart (as for soft drinks), or instead of by the gallon (as for gasoline).

**Soft Metric** - The result of a mathematical conversion of inch-pound measurements to metric equivalents for a particular purpose. The physical characteristics are not changed.

**Dual Systems** - The use of both inch-pound and metric systems. For example, an item is designed, produced, and described in inch-pound values with soft metric values also shown for information or comparison purposes.

(8) **Care of Live Vertebrate Animals**

a. The following notice is applicable when contract performance is expected to involve care of live vertebrate animals:

Notice to Offerors of Requirement for Adequate Assurance of Protection of Vertebrate Animal Subjects - (SEPTEMBER 1985)

The Public Health Service (PHS) Policy on Human Care and Use of Laboratory Animals establishes a number of requirements for research activities involving animals. Before a PHS award may be made to an applicant organization, the organization shall file, with the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), PHS, a written Animal Welfare Assurance which commits the organization to comply with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, the Animal Welfare Act, and the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources. In accordance with the PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, applicant organizations must

establish a committee, qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities and procedures. No PHS award involving the use of animals shall be made unless the Animal Welfare Assurance has been approved by OER. Prior to award, the Contracting Officer will notify Contractor(s) selected for projects that involve live vertebrate animals that an Animal Welfare Assurance is required. The Contracting Officer will request that OER, OLAW negotiate an acceptable Animal Welfare Assurance with those Contractor(s). For further information, OER, OLAW, may be contacted at Rockledge Center I - Suite 1050, 6705 Rockledge Drive, Bethesda, MD 20817, (301) 496-7163, ext 234. FAX copies are of the PHS Policy are available at (301) 402-2803. This policy is also available on the internet at http://www.grants.nih.gov/grants/olaw/olaw.htm.

b. If an Animal Assurance is already in place, the offeror's proposal shall include:

-The Animal Welfare Assurance number.
-The date last certified by OLAW. (i.e. assurance letter from OLAW)
-Evidence of recent AAALAC Accreditation.

(9) **Privacy Act (Treatment of Proposal Information)**

The Privacy Act of 1974 (P.L. 93-579) requires that a Federal agency advise each individual whom it asks to supply information, the authority which authorizes the solicitation, whether disclosure is voluntary or mandatory, the principal purpose or purposes for which the information is intended to be used, the uses outside the agency which may be made of the information, and the effects on the individual, if any, of not providing all or any part of the requested information.

The NIH is requesting the information called for in this RFP pursuant to the authority provided by Sec. 301(a)(7) of the Public Health Service Act, as amended, and P.L. 92-218, as amended.

Providing the information requested is entirely voluntary. The collection of this information is for the purpose of conducting an accurate, fair, and adequate review prior to a discussion as to whether to award a contract.

Failure to provide any or all of the requested information may result in a less than adequate review.

In addition, the Privacy Act of 1974 (P.L. 93-579, Section 7) requires that the following information be provided when individuals are requested to disclose their social security number.

Provision of the social security number is voluntary. Social security numbers are requested for the purpose of accurate and efficient identification, referral, review and management of NIH contracting programs. Authority for requesting this information is provided by Section 301 and Title IV of the PHS Act, as amended.

The information provided by you may be routinely disclosed for the following purposes:

- to the cognizant audit agency and the General Accounting Office for auditing.
- to the Department of Justice as required for litigation.
- to respond to congressional inquiries.
- to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

(10) **Selection of Offerors**

a) The acceptability of the scientific and technical portion of each research contract proposal will be evaluated by a technical review committee. The committee will evaluate each proposal in strict conformity with the evaluation criteria of the RFP, utilizing point scores and written critiques. The committee may suggest that the Contracting Officer request clarifying information from an offeror.

b) The business portion of each contract proposal will be subjected to a cost and price analysis, management analysis, etc.

c) If award will be made without conducting discussions, offerors may be given the opportunity to clarify certain aspects of their proposal (e.g., the relevance of an offeror's past performance information and adverse past performance information to which the offeror has not previously had an opportunity to respond) or to resolve minor or clerical errors.

d) If the Government intends to conduct discussions prior to awarding a contract-

(1) Communications will be held with offerors whose past performance information is the determining factor preventing them from being placed within the competitive range. Such communications shall address adverse past performance information to which an offeror has not had a prior opportunity to respond. Also, communications may be held with any other offerors whose exclusion from, or inclusion in, the competitive range is uncertain.

Such communications shall not be used to cure proposal deficiencies or omissions that alter the technical or cost elements of the proposal, and/or otherwise revise the proposal, but may be considered in rating proposals for the purpose of establishing the competitive range.

(2) The Contracting Officer will, in concert with program staff, decide which proposals are in the competitive range. The competitive range will be comprised of all of the most highly rated proposals. Oral or written discussions will be conducted with all offerors in the competitive range.

While it is this Institute's policy to conduct discussions with all offerors in the competitive range, the Institute reserves the right, in special circumstances, to limit the number of proposals included in the competitive range to the greatest number that will permit an efficient competition. All aspects of the proposals are subject to discussions, including cost, technical approach, past performance, and contractual terms and conditions. At the conclusion of discussions, each offeror still in the competitive range shall be given an opportunity to submit a written Final Proposal Revision (FPR) with the reservation of the right to conduct finalization of details with the selected sources in accordance with HHSAR 315.370.

e) The process described in FAR 15.101-1 will be employed, which permits the Government to make tradeoffs among cost or price and non-cost factors and to consider award to other than the lowest price offeror or other than the highest technically rated offeror. This process will take into consideration the results of the technical evaluation, the past performance evaluation (if applicable) and the cost analysis.

f) The Institute reserves the right to make a single award, multiple awards, or no award at all to the RFP. In addition, the RFP may be amended or canceled as necessary to meet the Institute's requirements. Synopses of awards exceeding $25,000 will be published in the FedBizOpps.

(11) **Salary Rate Limitation in Fiscal Year 2002** **

Offerors are advised that pursuant to P.L. 107-116, no NIH Fiscal Year 2002 (October 1, 2001 - September 30, 2002) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level I* (direct salary is exclusive of Overhead, Fringe Benefits and General and Administrative expenses, also referred to as "indirect cost" or "facilities and administrative (F&A) costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual compensation that the contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patient care or other activities. Direct salary (or institutional base salary) excludes any income that an individual may be permitted to earn outside of duties to the contractor.

This does not preclude the offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level I*. The salary rate limitation set by P.L. 107-116 applies only to Fiscal Year 2002 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level I* annual salary rate limit also applies to individuals proposed under subcontracts, however it does not apply to consultants. P.L. 107-116 states in pertinent part:

"None of the funds appropriated in this Act for the National Institutes of Health, the Agency for Healthcare Research and Quality, and the Substance Abuse, and Mental Health Services Administration shall be used to pay the salary of an individual through a grant or extramural mechanism at a rate in excess of Executive Level I."

**Information regarding the FY-2002 rate can be found at: http://www.opm.gov/oca/02tables/ex.pdf**

(12) **ROTC Access and Federal Military Recruiting on Campus**

Section 514 of the FY 1997 Appropriations Act prohibits NIH from providing contract funds to educational institutions that the Secretary of Defense determines have a policy or practice (regardless of when implemented ) that either prohibits, or in effect prevents (1) the maintaining, establishing, or operation of a unit of the Senior Reserve Officer Training Corps at the covered education entity; or (2) a student at the covered educational entity from enrolling in a unit of the Senior Reserve Officer Training Corps at another institution of higher education.

Further, contract funds may not be provided to educational institutions that have a policy or practice that prohibits or prevents (1) entry to campuses, or access to students (who are 17 years of age or older) on campuses, for purposes of Federal military recruiting; or (2) access by military recruiters for purposes of Federal military recruiting to information pertaining to students (who are 17 years of age or older) enrolled at the covered educational entity.

(13) **Solicitation Provisions Incorporated by Reference**, FAR 52.252-1 (February 1998)

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. The offeror is cautioned that the listed provisions may include blocks that must be completed by the offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a) Facilities Capital Cost of Money, FAR Clause 52.215-16, (October 1997).

b) Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).

c) Preaward On-Site Equal Opportunity Compliance Evaluation, (Over $10,000,000), FAR Clause 52.222-24, (February 1999).

**TECHNICAL PROPOSAL INSTRUCTIONS**

A detailed work plan must be submitted indicating how each aspect of the statement of work is to be accomplished. Your technical approach should be in as much detail as you consider necessary to fully explain your proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken. The technical proposal must include information on how the project is to be organized, staffed, and managed. Information should be provided which will demonstrate your understanding and management of important events or tasks.

(1) **Technical Discussions**

The technical discussion included in the technical proposal should respond to the items set forth below:

a) **Statement of Work**

(1) Objectives

State the overall objectives and the specific accomplishments you hope to achieve. Indicate the rationale for your plan, and relation to comparable work in progress elsewhere. Review pertinent work already published which is relevant to this project and your proposed approach. This should support the scope of the project as you perceive it.

(2) Approach

Use as many subparagraphs, appropriately titled, as needed to clearly outline the general plan of work. Discuss phasing of research and, if appropriate, include experimental design and possible or probable outcome of approaches proposed.

(3) Methods

Describe in detail the methodologies you will use for the project, indicating your level of experience with each, areas of anticipated difficulties, and any unusual expenses you anticipate.

(4) Schedule

Provide a schedule for completion of the work and delivery of items specified in the statement of work. Performance or delivery schedules shall be indicated for phases or segments, as applicable, as well as for the overall program. Schedules shall be shown in terms of calendar months from the date of authorization to proceed or, where applicable, from the date of a stated event, as for example, receipt of a required approval by the Contracting Officer. Unless the request for proposal indicates that the stipulated schedules are mandatory, they shall be treated as desired or recommended schedules. In this event, proposals based upon the offeror's best alternative schedule, involving no overtime, extra shift or other premium, will be accepted for consideration.

b) **Personnel**

Describe the experience and qualifications of personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program.

**OFFERORS SHOULD ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.**

(1) Principal Investigator/Project Director

List the name of the Principal Investigator/Project Director responsible for overall implementation of the contract and key contact for technical aspects of the project. Even though there may be co-investigators, identify the Principal Investigator/Project Director who will be responsible for the overall implementation of any awarded contract. Discuss the qualifications, experience, and accomplishments of the Principal Investigator/Project Director. State the estimated time to be spent on the project, his/her proposed duties, and the areas or phases for which he/she will be responsible.

(2) Other Investigators

List all other investigators/professional personnel who will be participating in the project. Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

(3) Additional Personnel

List names, titles, and proposed duties of additional personnel, if any, who will be required for full-time employment, or on a subcontract or consultant basis. The technical areas, character, and extent of subcontract or consultant activity will be indicated and the anticipated sources will be specified and qualified. For all proposed personnel who are not currently members of the offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement. Commitment letters for use of consultants and other personnel to be hired must include:

- The specific items or expertise they will provide.
- Their availability to the project and the amount of time anticipated.
- Willingness to act as a consultant.
- How rights to publications and patents will be handled.

(4) Resumes

Resumes of all key personnel are required. Each must indicate educational background, recent experience, specific or technical accomplishments, and a listing of relevant publications.

(2) **Technical Evaluation**

Proposals will be technically evaluated in accordance with the factors, weights, and order of relative importance as described in the Technical Evaluation Criteria (SEE SECTION M).

(3) **Additional Technical Proposal Information**

a) Proposals which merely offer to conduct a program in accordance with the requirements of the Government's scope of work will not be eligible for award. The offeror must submit an explanation of the proposed technical approach in conjunction with the tasks to be performed in achieving the project objectives.

b) The technical evaluation is conducted in accordance with the weighted technical evaluation criteria by an initial review panel. This evaluation produces a numerical score (points) which is based upon the information contained in the offeror's proposal only.

(4) **Other Considerations**

Record and discuss specific factors not included elsewhere which support your proposal. Using specifically titled subparagraphs, items may include:

a) Any agreements and/or arrangements with subcontractor(s). Provide as much detail as necessary to explain how the statement of work will be accomplished within this working relationship.

b) Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

c) Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.

d) Other factors you feel are important and support your proposed research.

e) Recommendations for changing reporting requirements if such changes would be more compatible with the offeror's proposed schedules.

BUSINESS PROPOSAL INSTRUCTIONS

(1) Basic Cost/Price Information

The business proposal must contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

(2) Qualifications of the Offeror

You are requested to submit a summary of your "General Experience, Organizational Experience Related to this RFP, Performance History and Pertinent Contracts."

a) **General Experience**

**General experience** is defined as general background, experience and qualifications of the offeror. A discussion of proposed facilities which can be devoted to the project may be appropriate.

b) **Organizational Experience Related to the RFP**

**Organizational experience** is defined as the accomplishment of work, either past or on-going, which is comparable or related to the effort required by this RFP. This includes overall offeror or corporate experience, **but not** the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in this RFP.

c) **Performance History**

**Performance history** is defined as meeting contract objectives within **delivery** and **cost schedules** on efforts, either past or on-going, which is comparable or related to the effort required by this RFP.

d) **Pertinent Contracts**

**Pertinent contracts** is defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

e) **Pertinent Grants**

List grants supported by the Government that involved similar or related work to that called for in this RFP. Include the grant number, involved agency, names of the grant specialist and the Science Administrator, identification of the work, and when performed.

You are cautioned that omission or an inadequate or inaccurate response to this very important RFP requirement could have a negative effect on the overall selection process. Experience and past performance are factors which are relevant to the ability of the offerors to perform and are considered in the source selection process.

(3) Other Administrative Data

a) **Property**

(1) It is DHHS policy that Contractors will provide all equipment and facilities necessary for performance of contracts. Exception may be granted to furnish Government-owned property, or to authorize purchase with contract funds, only when approved by the Contracting Officer. If the offeror is proposing that the

Government provide any equipment, other than that specified under Government Furnished Property in the RFP, the proposal must include comprehensive justification which includes:

(a) An explanation that the item is for a special use essential to the direct performance of the contract and the item will be used exclusively for the purpose. Office equipment such as desks, office machines, etc., will not be provided under a contract except under very exceptional circumstances.

(b) No practical or economical alternative exists (e.g., rental, capital investment) that can be used to perform the work.

(2) The offeror shall identify Government-owned property in its possession and/or Contractor titled property acquired from Federal funds, which it proposes to use in the performance of the prospective contract.

(3) The management and control of any Government property shall be in accordance with DHHS Publication (OS) 686 entitled, "Contractors Guide for Control of Government Property (1990)," a copy of which will be provided upon request.

b) **Submission of Electronic Funds Transfer Information with Offer, FAR Clause 52.232-38** (MAY 1999)

The offeror shall provide, with its offer, the following information that is required to make payment by electronic funds transfer (EFT) under any contract that results from this solicitation. This submission satisfies the requirement to provide EFT information under paragraphs (b)(1) and (j) of the clause at 52.232-34, Payment by Electronic Funds Transfer--Other than Central Contractor Registration.

(1) The solicitation number (or other procurement identification number).
(2) The offeror's name and remittance address, as stated in the offer.
(3) The signature (manual or electronic, as appropriate), title, and telephone number of the offeror's official authorized to provide this information.
(4) The name, address, and 9-digit Routing Transit Number of the offeror's financial agent.
(5) The offeror's account number and the type of account (checking, savings, or lockbox).
(6) If applicable, the Fedwire Transfer System telegraphic abbreviation of the offeror's financial agent.
(7) If applicable, the offeror shall also provide the name, address, telegraphic abbreviation, and 9-digit Routing Transit Number of the correspondent financial institution receiving the wire transfer payment if the offeror's financial agent is not directly on-line to the Fedwire and, therefore, not the receiver of the wire transfer payment.

c) **Financial Capacity**

The offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source.

(4) Subcontractors

If subcontractors are proposed, please include a commitment letter from the subcontractor detailing:

a) Willingness to perform as a subcontractor for specific duties (list duties).

b) What priority the work will be given and how it will relate to other work.

c) The amount of time and facilities available to this project.

d) Information on their cognizant field audit offices.

e) How rights to publications and patents are to be handled.

f) A complete cost proposal in the same format as the offeror's cost proposal.

Note: Organizations that plan to enter into a subcontract with an educational concern under a contract awarded under this RFP should refer to the following Web Site for a listing of clauses that are required to be incorporated in Research & Development (R&D) subcontracts with educational institutions:

http://ocm.od.nih.gov/contracts/rfps/FDP/PDPclausecover.htm

(5) Proposer's Annual Financial Report

*****This document is INCLUDED in the "Just In Time" procedures. Specific instructions for the submission of this document are outlined in SECTION L.1.a. of this RFP. *****

All offerors included in the competitive range will be required to submit a copy of the organization's most recent annual financial report.

*****(IF JUST IN TIME IS NOT BEING USED FOR THIS SOLICITATION USE THE FOLLOWING LANGUAGE IN LIEU OF THE ABOVE.) *****

A copy of the organization's most recent annual report must be submitted as part of the business proposal.

(6) Representations and Certifications

One copy of the Representations and Certifications attached as Section K shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of the Representations and Certifications shall be submitted from any proposed subcontractor.

(7) Travel Costs/Travel Policy

a) **Travel Policy**

*****This document is INCLUDED in the "Just In Time" procedures. Specific instructions for the submission of this document are outlined in SECTION L.1.a. of this RFP. *****

All offerors included within the competitive range will be required to submit one copy of their written travel policy. A written travel policy for any proposed subcontractors shall also be submitted at that time. If an offeror (or any proposed subcontractor) does not have a written travel policy, the offeror shall so state.

*****(IF "JUST IN TIME" IS NOT BEING USED FOR THIS SOLICITATION USE THE FOLLOWING LANGUAGE IN LIEU OF THE ABOVE.) *****

One copy of the offeror's (and any proposed subcontractor's) written travel policy shall be included in the business proposal (original only). If an offeror (or any proposed subcontractor) does not have a written travel policy, the offeror shall so state.

# SECTION M - EVALUATION FACTORS FOR AWARD

**New Animal Models for: Part A Tuberculosis (TB) and Invasive Aspergillosis (IA)**
**DMID-03-09**

## 1. GENERAL

The technical proposal will receive paramount consideration in the selection of the Contractor(s) for this acquisition. All evaluation factors, other than cost or price, when combined are significantly more important than cost or price. However, cost/price may become a critical factor in source selection in the event that two or more offerors are determined to be essentially equal following the evaluation of all factors other than cost or price. In any event, the Government reserves the right to make an award(s) to that offeror(s) whose proposal provides the best overall value to the Government.

## 2. MANDATORY QUALIFICATION CRITERIA

Listed below are mandatory qualification criteria. [THE OFFEROR SHALL INCLUDE ALL INFORMATION WHICH DOCUMENTS AND/OR SUPPORTS THE QUALIFICATION CRITERIA IN ONE CLEARLY MARKED SECTION OF ITS PROPOSAL/THE OFFEROR SHALL PROVIDE AN INDEX WITHIN ITS PROPOSAL WHICH DIRECTS THE REVIEWER(S) TO THE SPECIFIC AREA(S) OF THE PROPOSAL THAT ADDRESS A PARTICULAR MANDATORY QUALIFICATION.]

**For Part A – NEW ANIMAL MODELS FOR TB:**

**The offeror shall, at the time of the proposal have available animal and laboratory facilities that allow research using virulent *Mycobacterium tuberculosis. Alternatively, the offeror shall provide in the proposal documentation clearly outlining arrangements that are in place to assure access to these facilities by the time the contract is awarded. These facilities shall include BSL3 containment of laboratory as well as animal research and animal holding. These facilities must be large enough, as documented by the inclusion of floor plans to accommodate routine testing of genes in animals and execution of all related methodologies and techniques. At the time of award, BSL3 facilities must be operational.***

The qualification criteria establishes conditions that must be met at the time of receipt of Final Proposal Revisions (FPRs) by the Contracting Officer in order for your proposal to be considered any further for award.

## 3. EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government's conclusions about overall commitment and realism of the offeror's SDB Participation targets will be used in determining the relative merits of the offeror's proposal and in selecting the offeror whose proposal is considered to offer the best value to the Government.

The extent of the offeror's Small Disadvantaged Business Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the offeror's proposal. The Government is seeking to determine whether the offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

(a) Extent to which SDB concerns are specifically identified
(b) Extent of commitment to use SDB concerns
(c) Complexity and variety of the work SDB concerns are to perform
(d) Realism of the proposal
(e) Past performance of offerors in complying with subcontracting plan goals for SDB concerns and monetary targets for SDB participation
(f) Extent of participation of SDB concerns in terms of the value of the total acquisition.

## 4. TECHNICAL EVALUATION CRITERIA

The evaluation criteria are used by the technical evaluation committee when reviewing the technical proposals. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

**CRITERA** **WEIGHT**

**1. TECHNICAL APPROACH PARTA–NEWANIMALMODELS FOR TB** **65 Points**

a. SCIENTIFIC MERIT AND TECHNICAL APPROACH TO THE DEVELOPMENT OF ANIMAL MODELS (30 Points)

Scientific merit, utilization of current techniques and feasibility of the technical approach are of critical importance.
Points to consider include:

- o Clear understanding of merits and weaknesses of currently accepted animal model to mimic various stages of *M. tuberculosis* (Mtb) infection and tuberculosis disease progression
- o Clear rationale for the selection of mycobacterial and animal strains and for the number and identity of genes used to validate the models
- o Suitability and quality of preliminary data to justify model approaches
- o Suitability of the proposed model(s) to follow disease progression
- o Suitability of genes used to validate the model(s) to answer questions regarding mycobacterial survival, host-pathogen interaction and host response to infection
- o Suitability of the genetic system used to engineer mycobacterial strains
- o Proposed timelines to develop the model(s) and make it available for testing
- o Presentation of alternative strategies and methodologies
- o Rationale for the development of multiple animal models if the function of Mtb genes cannot be determined in one model.
- o Rationale and approach to manipulating Mtb strains by genetic means to allow identification of the role of individual gene products
- o Expected outcomes from various proposed strategies
- o Amenability to gene expression profiling

b. SUITABILITY OF THE PROPOSED MODELS FOR TESTING OF LARGE NUMBERS OF TARGET GENES (25 Points)

The design of the model(s) must take into consideration that it is to be used for routine evaluation of target genes. Aspects of the model that make it suitable for testing large numbers of target genes in rapid throughput format must be evaluated.
Points to consider include:

- o Resource and time requirements to evaluate the function of a specific gene and suitability of this design for rapid throughput evaluation
- o Number of animals required for each experiment
- o Strategies for genetic manipulation of mycobacterial strains to allow routine manipulation and cloning of target genes
- o Inclusion of appropriate controls

c. SUITABILITY AND FEASIBILITY OF PLANS FOR ADMINISTRATION, MANAGEMENT AND QUALITY CONTROL PROCEDURES (10 Points)

Detailed description of administrative framework must be provided showing clear lines of authority, and how staff resources will be adjusted to accommodate model development as well as testing as part of WORK STATEMENT, Part A, 3). Draft SOPs and procedures for implementing the contract shall also be evaluated. Applicability of the draft SOPs to the overall goal of the contract, which is to fill a critical gap between genomic and translational research is to be considered. Quality and content of the training plan shall be evaluated for its suitability to fill training needs as outlined in the Statement of Work.

**2. PERSONNEL QUALIFICATIONS PART A** **25 Points**

Documented training, experience and qualifications of the proposed personnel in working with infectious diseases and animal models will be evaluated. Proposals will be judged on the basis of experience and current participation of personnel in programs similar to that described in the Work Statement. The proposed research team, which may include sub-contractors, shall, as a whole, provide all necessary expertise to perform work under this contract. Expertise of the sub-contractor(s) is to be evaluated under 2. OTHER PERSONNEL/STAFFING PLAN.

1. PRINCIPAL INVESTIGATOR (10 Points)

The academic training and experience of the principal investigator must be appropriate to conduct this contract.
Points to consider include:

- o Relevance and quality of recent work in the area of mycobacterial infections.
- o Expertise in mycobacterial biology, genetics, molecular biology and animal models of Mtb infection and tuberculosis.
- o Documented ability to manage the proposed project in relation to other commitments.

2. OTHER PERSONNEL/STAFFING PLAN (15 Points)

Points to consider include:

- o Relevant experience and documented skills of other professional and technical staff, including sub-contractors, in mycobacterial biology, genetics, general molecular biological techniques and animal modeling with Mtb.
- o Adequacy of the staffing plan, including provisions to conduct this model as a service to the community.
- o Plans to accommodate fluctuations in workload

**3. FACILITIES AND RESOURCES PART A** **10 Points**

Offerors will be evaluated on the suitability, availability and accessibility of laboratory and animal housing space, major equipment and physical facilities required to conduct the proposed studies in a timely and efficient manner. This includes the availability of sufficient laboratory and animal space under appropriate (BSL2/3) biosafety containment for the proposed experiments. Adequate equipment and computing infrastructure must be available to perform microarray experiments/gene profiling if these experiments are part of the proposal.

**TOTAL PART A** **100 Points**

**1. TECHNICAL APPROACH PARTB–NEWANIMALMODELS FOR INVASIVE ASPERGILLOSIS 65 Points**

a. SCIENTIFIC MERIT AND TECHNICAL APPROACH TO THE DEVELOPMENT OF ANIMAL MODELS (40 Points)

Scientific merit, utilization of current techniques and feasibility of the technical approach are of critical importance.
Points to consider include:

- o Demonstrated expertise of the offeror to develop animal models of aspergillosis
- o Clear understanding of currently available models
- o Proposed timelines to develop the model and make it available for testing
- o Amenability to assessing growth dynamics of filamentous fungi
- o Suitability of the proposed model(s) to allow continuous blood sampling.
- o Suitability of the proposed model(s) to evaluate surrogate markers of infection.
- o Suitability of the proposed model(s) to follow disease progression
- o Presentation of alternative methodologies
- o Rationale for the development of multiple animal models of aspergillosis
- o Expected outcomes from various proposed strategies
- o Amenability to gene expression profiling

b. SUITABILITY OF THE PROPOSED MODELS TO ANSWER SCIENTIFIC QUESTIONS AS A SERVICE TO THE COMMUNITY (15 Points)

The design of the model(s) must take into consideration that it is to be used to answer specific questions as determined by gaps identified in research. For this, the model(s) is expected to have adequate flexibility.
Points to consider include:

- o Duration of the model should be such that the lifespan of the infected animals is suitable to characterize surrogate markers of infection and disease progression as distinguished from colonization or prior exposure
- o Number of animals required for each experiment

d. SUITABILITY AND FEASIBILITY OF PLANS FOR ADMINISTRATION, MANAGEMENT AND QUALITY CONTROL PROCEDURES (10 Points)

Detailed description of administrative framework must be provided showing clear lines of authority, and how staff resources will be adjusted to accommodate model development as well as conducting models as a service to the research community. Draft SOPs and procedures for implementing the contract shall also be evaluated. Applicability of the draft SOPs to the overall goal of the contract, which is to answer key scientific questions and validate information that is expected from the sequencing of *Aspergillus fumigatus* and related genomes. Quality and content of the training plan shall be evaluated for its suitability to fill training needs as outlined in the Statement of Work.

**2. PERSONNEL QUALIFICATIONS PART B** **25 Points**

Documented training, experience and qualifications of the proposed personnel in working with infectious diseases and animal models will be evaluated. Proposals will be judged on the basis of experience and current participation of personnel in programs similar to that described in the Work Statement. The proposed research team, which may include sub-contractors, shall, as a whole, provide all necessary expertise to perform work under this contract. Expertise of the sub-contractor(s) is to be evaluated under 2. OTHER PERSONNEL/STAFFING PLAN.

1. PRINCIPAL INVESTIGATOR (10 Points)

The academic training and experience of the principal investigator must be appropriate to conduct this contract.
Points to consider include:

- o Relevance and quality of recent work in the area of fungal infections in animal models
- o Documented ability to manage the proposed project in relation to other commitments

2. OTHER PERSONNEL/STAFFING PLAN (15 Points)

Points to consider include:

- o Relevant experience and documented skills of other professional and technical staff, including sub-contractors.
- o Adequacy of the staffing plan, including provisions to conduct this model as a service to the community .
- o Plans to accommodate fluctuations in workload.

**3. FACILITIES AND RESOURCES Part B** **10 Points**

Offerors will be evaluated on the suitability, availability and accessibility of laboratory and animal housing space, major equipment and physical facilities required to conduct the proposed studies in a timely and efficient manner. This includes the availability of sufficient laboratory and animal space under BSL2 containment.

**TOTAL PART B** **100 Points**